



## Complete Summary

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### GUIDELINE TITLE

ACC/AHA 2007 guidelines for the management of patients with unstable angina/non ST-Elevation myocardial infarction.

### BIBLIOGRAPHIC SOURCE(S)

Anderson JL, Adams CD, Antman EM, Bridges CR, Califf RM, Casey DE Jr, Chavey WE 2nd, Fesmire FM, Hochman JS, Levin TN, Lincoff AM, Peterson ED, Theroux P, Wenger NK, Wright RS, Smith SC Jr, Jacobs AK, Adams CD, Anderson JL, Antman EM, Halperin JL, Hunt SA, Krumholz HM, Kushner FG, Lytle BW, Nishimura R, Ornato JP, Page RL, Riegel B, American College of Cardiology, American Heart Association Task Force on Practice Guidelines (Writing Committee, American College of Emergency Physicians, Society for Cardiovascular Angiography and Interventions, Society of Thoracic Surgeons, American Association of Cardiovascular and Pulmonary Rehabilitation, Society for Academic Emergency Medicine. ACC/AHA 2007 guidelines for the management of patients with unstable angina/non-ST-Elevation myocardial infarction: a report of the American College of Cardiology. J Am Coll Cardiol 2007 Aug 14;50(7):e1-e157. [957 references] [PubMed](#)

### GUIDELINE STATUS

This is the most current release of the guideline.

This guideline updates a previous version: American College of Cardiology Foundation, American Heart Association. ACC/AHA guidelines for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Bethesda (MD): American College of Cardiology Foundation (ACCF); 2002 Mar. 95 p.

### **\*\* REGULATORY ALERT \*\***

### FDA WARNING/REGULATORY ALERT

**Note from the National Guideline Clearinghouse:** This guideline references a drug(s)/intervention(s) for which important revised regulatory and/or warning information has been released.

- [February 28, 2008, Heparin Sodium Injection](#): The U.S. Food and Drug Administration (FDA) informed the public that Baxter Healthcare Corporation has voluntarily recalled all of their multi-dose and single-use vials of heparin sodium for injection and their heparin lock flush solutions. Alternate heparin manufacturers are expected to be able to increase heparin production

- sufficiently to supply the U.S. market. There have been reports of serious adverse events including allergic or hypersensitivity-type reactions, with symptoms of oral swelling, nausea, vomiting, sweating, shortness of breath, and cases of severe hypotension.
- [August 16, 2007, Coumadin \(Warfarin\)](#): Updates to the labeling for Coumadin to include pharmacogenomics information to explain that people's genetic makeup may influence how they respond to the drug.
  - [June 8, 2007, Troponin-I Immunoassay](#): Class I Recall of all lots of the Architect Stat Troponin-I Immunoassay. The assay may report falsely elevated or falsely decreased results at and near a low level, which may impact patient treatment.

## COMPLETE SUMMARY CONTENT

\*\* REGULATORY ALERT \*\*

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## SCOPE

### DISEASE/CONDITION(S)

- Coronary artery disease
- Unstable angina
- Non-ST-segment elevation myocardial infarction

### GUIDELINE CATEGORY

Diagnosis

Evaluation

Management

Prevention

Risk Assessment

Treatment

### CLINICAL SPECIALTY

Cardiology

Emergency Medicine

Family Practice

Geriatrics

Internal Medicine  
Thoracic Surgery

## **INTENDED USERS**

Health Care Providers  
Physicians

## **GUIDELINE OBJECTIVE(S)**

- To address the diagnosis and management of patients with unstable angina (UA) and the closely related condition of non-ST-elevation myocardial infarction (NSTEMI)
- To assist both cardiovascular specialists and nonspecialists in the proper evaluation and management of patients with an acute onset of symptoms suggestive of these conditions
- To provide recommendations and supporting evidence for the continued management of patients with these conditions in both inpatient and outpatient settings

## **TARGET POPULATION**

Adult patients with unstable angina and non-ST-segment elevation myocardial infarction (UA/NSTEMI)

Special populations considered include women, patients with diabetes mellitus, post-coronary artery bypass (CABG) patients, older adults, patients with chronic kidney disease, cocaine and methamphetamine users, patients with variant (Prinzmetal's) angina, patients with Cardiovascular "Syndrome X" and patients with Takotsubo Cardiomyopathy.

Excluded from these guidelines are:

- Patients diagnosed as having ST-elevation myocardial infarction (STEMI). These patients should be managed as indicated according to the American College of Cardiology/American Heart Association (ACC/AHA) Guidelines for Management of Patients with Acute Myocardial Infarction. (Patients with acute myocardial infarction and with definite ischemic electrocardiogram changes who are not suitable for acute reperfusion should be diagnosed and managed as patients with unstable angina.)
- Patients who experience periprocedural myocardial damage that is reflected in release of the MB isoenzyme of creatine kinase (CK-MB) or troponin

## **INTERVENTIONS AND PRACTICES CONSIDERED**

### **Initial Evaluation and Management**

1. Clinical assessment, including 12-lead electrocardiogram, biomarker determination, physical examination, and stress test
2. Instructions to call 9-1-1 if signs of acute coronary syndrome
3. Pre-hospital aspirin (ASA) and nitroglycerin (NTG) as appropriate

4. Risk stratification

### **Early Hospital Care**

1. Anti-ischemic and analgesic therapy, including NTG, beta blockers, angiotensin-converting enzyme (ACE) inhibitors, calcium channel blockers, angiotensin receptor blocker (ARB), morphine sulfate, long-acting nondihydropyridine calcium antagonists, supplemental oxygen
2. Anti-platelet and anticoagulant therapy, including ASA, clopidogrel, glycoprotein (GP) IIb/IIIa inhibitors, enoxaparin, unfractionated heparin (UFH)
3. Consideration of conservative versus invasive initial strategies
4. Risk stratification at discharge

### **Revascularization**

1. Percutaneous coronary intervention (PCI)
2. Coronary artery bypass graft (CABG) surgery

### **Post-Discharge Care**

1. Continuation of medications to control ischemia
2. Long-term medical therapy, including anti-platelet therapy, beta blockers, inhibitors of the rennin-angiotensins-aldosterone system (ACE inhibitors, ARBs), NTG, calcium channel blockers, warfarin
3. Secondary prevention, including lipid management, blood pressure control, treatment of diabetes mellitus, smoking cessation, weight management, physical activity, patient education, influenza immunization, depression screening, and pain relief
4. Post-discharge follow-up and cardiac rehabilitation
5. Consideration of special groups

### **MAJOR OUTCOMES CONSIDERED**

- Sensitivity, specificity, and accuracy of diagnostic tests
- Risk of death or nonfatal myocardial infarction
- Morbidity and mortality associated with unstable angina and non-ST-segment elevation myocardial infarction
- Quality of life

## **METHODOLOGY**

### **METHODS USED TO COLLECT/SELECT EVIDENCE**

Hand-searches of Published Literature (Primary Sources)  
Searches of Electronic Databases

### **DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE**

The committee members reviewed and compiled published reports through a series of computerized literature searches of the English-language literature since 2002 and a final manual search of selected articles. Details of the specific searches conducted for particular sections are provided in the original guideline document when appropriate. Detailed evidence tables were developed whenever necessary with the specific criteria outlined in the individual sections of the original guideline document.

## NUMBER OF SOURCE DOCUMENTS

Not stated

## METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

## RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

### Applying Classification of Recommendations and Level of Evidence

		SIZE OF TREATMENT EFFECT		
		CLASS I	CLASS IIa	CLASS IIb
		<i>Benefit &gt;&gt;&gt; Risk</i>  Procedure/Treatment <b>SHOULD</b> be performed/ administered	<i>Benefit &gt;&gt; Risk</i> <i>Additional studies with focused objectives needed</i>  <b>IT IS REASONABLE</b> to perform procedure/ administer treatment	<i>Benefit ≥ Risk</i> <i>Additional studies with focused objectives needed</i> <i>registry or clinical trial would be helpful</i>  Procedure/Treatment <b>BE CONSIDERED</b>
Estimate of Certainty (Precision) of Treatment Effect	LEVEL A	<ul style="list-style-type: none"> <li>Recommendation that procedure or treatment is useful/effective</li> <li>Sufficient evidence from multiple randomized trials or meta-analyses</li> </ul>	<ul style="list-style-type: none"> <li>Recommendation in favor of treatment of procedure being useful/effective</li> <li>Some conflicting evidence from multiple randomized trials or meta-analyses</li> </ul>	<ul style="list-style-type: none"> <li>Recommendation in favor of treatment of procedure being useful/effective</li> <li>Some conflicting evidence from multiple randomized trials or meta-analyses</li> </ul>

		SIZE OF TREATMENT EFFECT		
		CLASS I	CLASS IIa	CLASS IIb
		<i>Benefit &gt;&gt;&gt; Risk</i>  Procedure/Treatment <b>SHOULD</b> be performed/ administered	<i>Benefit &gt;&gt; Risk</i> <i>Additional studies with focused objectives needed</i>  <b>IT IS REASONABLE</b> to perform procedure/ administer treatment	<i>Benefit ≥ Risk</i> <i>Additional studies with objective endpoints, registry or observational data helpful</i>  Procedure/Treatment <b>BE CONSIDERED</b>
	LEVEL B	<ul style="list-style-type: none"> <li>Recommendation that procedure or treatment is useful/effective</li> <li>Limited evidence from single randomized trial or nonrandomized studies</li> </ul>	<ul style="list-style-type: none"> <li>Recommendation in favor of treatment of procedure being useful/effective</li> <li>Some conflicting evidence from single randomized trial or nonrandomized studies</li> </ul>	<ul style="list-style-type: none"> <li>Recommendation in favor of treatment of procedure being useful/effective</li> <li>Only diverging expert opinion, case studies, or standard-of-care</li> </ul>
	LEVEL C	<ul style="list-style-type: none"> <li>Recommendation that procedure or treatment is useful/effective</li> <li>Only expert opinion, case studies, or standard-of-care</li> </ul>	<ul style="list-style-type: none"> <li>Recommendation in favor of treatment of procedure being useful/effective</li> <li>Only diverging expert opinion, case studies, or standard-of-care</li> </ul>	<ul style="list-style-type: none"> <li>Recommendation in favor of treatment of procedure being useful/effective</li> <li>Only expert opinion, case studies, or standard-of-care</li> </ul>

\*Data available from clinical trials or registries about the usefulness/efficacy in different subpopulations, such as gender, age, history of diabetes, history of prior myocardial infarction, history of heart failure, and prior aspirin use. A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Even though randomized trials are not available, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

NOTE: In 2003, the American College of Cardiology/American Heart Association (ACC/AHA) Task Force on Practice Guidelines developed a list of suggested phrases to use when writing recommendations. All guideline recommendations have been written in full sentences that express a complete thought, such that a recommendation, even if separated and presented apart from the rest of the document (including headings above sets of recommendations), would still convey the full intent of the recommendation. It is hoped that this will increase readers' comprehension of the guidelines and will allow queries at the individual recommendation level. (See Table 1 in the original guideline document for a list of suggested phrases for writing recommendations.)

## **METHODS USED TO ANALYZE THE EVIDENCE**

Meta-Analysis of Randomized Controlled Trials  
Review of Published Meta-Analyses  
Systematic Review with Evidence Tables

## **DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE**

Detailed evidence tables were developed whenever necessary with the specific criteria outlined in the individual sections of the original guideline document.

## **METHODS USED TO FORMULATE THE RECOMMENDATIONS**

Expert Consensus

## **DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS**

Experts in the subject under consideration have been selected from both organizations (the American College of Cardiology and the American Heart Association) to examine subject-specific data and write guidelines. The process includes additional representatives from other medical practitioner and specialty groups when appropriate. Writing committees are specifically charged to perform a formal literature review, weigh the strength of evidence for or against a particular treatment or procedure, and include estimates of expected health outcomes where data exist. Patient-specific modifiers, comorbidities, and issues of patient preference that might influence the choice of particular tests or therapies are considered, as well as frequency of follow-up and cost effectiveness. When available, information from studies on cost will be considered; however, review of data on efficacy and clinical outcomes will constitute the primary basis for preparing recommendations in these guidelines.

## **RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS**

See the "Rating Scheme for the Strength of the Evidence" field above.

## **COST ANALYSIS**

Guideline developers reviewed published cost analyses.

## **METHOD OF GUIDELINE VALIDATION**

External Peer Review  
Internal Peer Review

## **DESCRIPTION OF METHOD OF GUIDELINE VALIDATION**

This guideline update was reviewed by 2 outside reviewers nominated by each of the American College of Cardiology (ACC) and American Heart Association (AHA) and by 49 peer reviewers.

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

The American College of Cardiology/American Heart Association (ACC/AHA) classification of the recommendations for patient evaluation and treatment (classes I-III) and the levels of evidence (A-C) are defined at the end of the Major Recommendations field.

#### **Identification of Patients at Risk of UA/NSTEMI**

##### *Class I*

1. Primary care providers should evaluate the presence and status of control of major risk factors for coronary heart disease (CHD) for all patients at regular intervals (approximately every 3 to 5 years). (*Level of Evidence: C*)
2. Ten-year risk (National Cholesterol Education Program [NCEP] global risk) of developing symptomatic CHD should be calculated for all patients who have 2 or more major risk factors to assess the need for primary prevention strategies (Grundy et al., 2004; Third Report of the NCEP Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults [Adult Treatment Panel III], 2002). (*Level of Evidence: B*)
3. Patients with established CHD should be identified for secondary prevention efforts, and patients with a CHD risk equivalent (e.g., atherosclerosis in other vascular beds, diabetes mellitus, chronic kidney disease, or 10-year risk greater than 20% as calculated by Framingham equations) should receive equally intensive risk factor intervention as those with clinically apparent CHD. (*Level of Evidence: A*)

#### **Initial Evaluation and Management**

##### **Clinical Assessment**

##### *Class I*

1. Patients with symptoms that may represent acute coronary syndrome (ACS) (see Table below) should not be evaluated solely over the telephone but should be referred to a facility that allows evaluation by a physician and the recording of a 12-lead electrocardiogram (ECG) and biomarker determination (e.g., an Emergency Department (ED) or other acute care facility). (*Level of Evidence: C*)
2. Patients with symptoms of ACS (chest discomfort with or without radiation to the arm[s], back, neck, jaw, or epigastrium; shortness of breath; weakness; diaphoresis; nausea; lightheadedness) should be instructed to call 9-1-1 and should be transported to the hospital by ambulance rather than by friends or relatives. (*Level of Evidence: B*)
3. Health care providers should actively address the following issues regarding ACS with patients with or at risk for CHD and their families or other responsible caregivers:
  - a. The patient's heart attack risk (*Level of Evidence: C*)
  - b. How to recognize symptoms of ACS (*Level of Evidence: C*)



- c. The advisability of calling 9-1-1 if symptoms are unimproved or worsening after 5 min, despite feelings of uncertainty about the symptoms and fear of potential embarrassment (*Level of Evidence: C*)
  - d. A plan for appropriate recognition and response to a potential acute cardiac event, including the phone number to access emergency medical services (EMS), generally 9-1-1 (Dracup et al., 1997) (*Level of Evidence: C*)
4. Prehospital EMS providers should administer 162 to 325 mg of aspirin (ASA) (chewed) to chest pain patients suspected of having ACS unless contraindicated or already taken by the patient. Although some trials have used enteric-coated ASA for initial dosing, more rapid buccal absorption occurs with non-enteric-coated formulations. (*Level of Evidence: C*)
  5. Health care providers should instruct patients with suspected ACS for whom nitroglycerin [NTG] has been prescribed previously to take not more than 1 dose of NTG sublingually in response to chest discomfort/pain. If chest discomfort/pain is unimproved or is worsening 5 min after 1 NTG dose has been taken, it is recommended that the patient or family member/friend/caregiver call 9-1-1 immediately to access EMS before taking additional NTG. In patients with chronic stable angina, if symptoms are significantly improved by 1 dose of NTG, it is appropriate to instruct the patient or family member/friend/caregiver to repeat NTG every 5 min for a maximum of 3 doses and call 9-1-1 if symptoms have not resolved completely. (*Level of Evidence: C*)
  6. Patients with a suspected ACS with chest discomfort or other ischemic symptoms at rest for greater than 20 min, hemodynamic instability, or recent syncope or presyncope should be referred immediately to an ED. Other patients with suspected ACS who are experiencing less severe symptoms and who have none of the above high-risk features, including those who respond to an NTG dose, may be seen initially in an ED or an outpatient facility able to provide an acute evaluation. (*Level of Evidence: C*)

**Table. Guidelines for the Identification of ACS Patients by ED Registration Clerks or Triage Nurses**

<b>Registration/Clerical Staff</b>
<p>Patients with the following chief complaints require immediate assessment by the triage nurse and should be referred for further evaluation:</p> <ul style="list-style-type: none"> <li>• Chest pain, pressure, tightness, or heaviness; pain that radiates to neck, jaw, shoulders, back, or 1 or both arms</li> <li>• Indigestion or "heartburn"; nausea and/or vomiting associated with chest discomfort</li> <li>• Persistent shortness of breath</li> <li>• Weakness, dizziness, lightheadedness, loss of consciousness</li> </ul>
<b>Triage Nurse</b>
<p>Patients with the following symptoms and signs require immediate assessment by the triage nurse for the initiation of the ACS protocol:</p> <ul style="list-style-type: none"> <li>• Chest pain or severe epigastric pain, nontraumatic in origin, with components</li> </ul>

<p>typical of myocardial ischemia or myocardial infarction (MI):</p> <ul style="list-style-type: none"> <li>• Central/substernal compression or crushing chest pain</li> <li>• Pressure, tightness, heaviness, cramping, burning, aching sensation</li> <li>• Unexplained indigestion, belching, epigastric pain</li> <li>• Radiating pain in neck, jaw, shoulders, back, or 1 or both arms</li> <li>• Associated dyspnea</li> <li>• Associated nausea and/or vomiting</li> <li>• Associated diaphoresis</li> </ul> <p>If these symptoms are present, obtain stat ECG.</p>
<p style="text-align: center;"><b>Medical History</b></p> <p>The triage nurse should take a brief, targeted, initial history with an assessment of current or past history of:</p> <ul style="list-style-type: none"> <li>• Coronary artery bypass graft surgery (CABG), percutaneous coronary intervention (PCI), coronary artery disease (CAD), angina on effort, or MI</li> <li>• NTG use to relieve chest discomfort</li> <li>• Risk factors, including smoking, hyperlipidemia, hypertension, diabetes mellitus, family history, and cocaine or methamphetamine use</li> <li>• Regular and recent medication use</li> </ul> <p>The brief history must not delay entry into the ACS protocol.</p>
<p style="text-align: center;"><b>Special Considerations</b></p> <p>Women may present more frequently than men with atypical chest pain and symptoms.</p> <p>Diabetic patients may have atypical presentations due to autonomic dysfunction.</p> <p>Elderly patients may have atypical symptoms such as generalized weakness, stroke, syncope, or a change in mental status.</p>

Adapted from National Heart Attack Alert Program. Emergency Department: rapid identification and treatment of patients with acute myocardial infarction. Bethesda, MD: US Department of Health and Human Services. US Public Health Service. National Institutes of Health. National Heart, Lung and Blood Institute, September 1993. NIH Publication No. 93-3278 (6).

### *Class IIa*

1. It is reasonable for health care providers and 9-1-1 dispatchers to advise patients without a history of ASA allergy who have symptoms of ACS to chew ASA (162 to 325 mg) while awaiting arrival of prehospital EMS providers. Although some trials have used enteric-coated ASA for initial dosing, more rapid buccal absorption occurs with non-enteric-coated formulations. (*Level of Evidence: B*)
2. It is reasonable for health care providers and 9-1-1 dispatchers to advise patients who tolerate NTG to repeat NTG every 5 min for a maximum of 3 doses while awaiting ambulance arrival. (*Level of Evidence: C*)
3. It is reasonable that all prehospital EMS providers perform and evaluate 12-lead ECGs in the field (if available) on chest pain patients suspected of ACS to assist in triage decisions. Electrocardiographs with validated computer-generated interpretation algorithms are recommended for this purpose. (*Level of Evidence: B*)

4. If the 12-lead ECG shows evidence of acute injury or ischemia, it is reasonable that prehospital ACLS providers relay the ECG to a predetermined medical control facility and/or receiving hospital. (*Level of Evidence: B*)

## **Early Risk Stratification**

### *Class I*

1. A rapid clinical determination of the likelihood risk of obstructive CAD (i.e., high, intermediate, or low) should be made in all patients with chest discomfort or other symptoms suggestive of an ACS and considered in patient management. (*Level of Evidence: C*)
2. Patients who present with chest discomfort or other ischemic symptoms should undergo early risk stratification for the risk of cardiovascular events (e.g., death or [re]MI) that focuses on history, including anginal symptoms, physical findings, ECG findings, and biomarkers of cardiac injury, and results should be considered in patient management. (*Level of Evidence: C*)
3. A 12-lead ECG should be performed and shown to an experienced emergency physician as soon as possible after ED arrival, with a goal of within 10 min of ED arrival for all patients with chest discomfort (or anginal equivalent) or other symptoms suggestive of ACS. (*Level of Evidence: B*)
4. If the initial ECG is not diagnostic but the patient remains symptomatic and there is high clinical suspicion for ACS, serial ECGs, initially at 15- to 30-min intervals, should be performed to detect the potential for development of ST-segment elevation or depression. (*Level of Evidence: B*)
5. Cardiac biomarkers should be measured in all patients who present with chest discomfort consistent with ACS. (*Level of Evidence: B*)
6. A cardiac-specific troponin is the preferred marker, and if available, it should be measured in all patients who present with chest discomfort consistent with ACS. (*Level of Evidence: B*)
7. Patients with negative cardiac biomarkers within 6 h of the onset of symptoms consistent with ACS should have biomarkers re-measured in the time frame of 8 to 12 h after symptom onset. (The exact timing of serum marker measurement should take into account the uncertainties often present with the exact timing of onset of pain and the sensitivity, precision, and institutional norms of the assay being utilized as well as the release kinetics of the marker being measured.) (*Level of Evidence: B*)
8. The initial evaluation of the patient with suspected ACS should include the consideration of noncoronary causes for the development of unexplained symptoms. (*Level of Evidence: C*)

### *Class IIa*

1. Use of risk-stratification models, such as the Thrombolysis In Myocardial Infarction (TIMI) or Global Registry of Acute Coronary Events (GRACE) risk score or the Platelet Glycoprotein IIb/IIIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy (PURSUIT) risk model, can be useful to assist in decision making with regard to treatment options in patients with suspected ACS. (*Level of Evidence: B*)
2. It is reasonable to remeasure positive biomarkers at 6- to 8-h intervals 2 to 3 times or until levels have peaked, as an index of infarct size and dynamics of necrosis. (*Level of Evidence: B*)

3. It is reasonable to obtain supplemental ECG leads V<sub>7</sub> through V<sub>9</sub> in patients whose initial ECG is nondiagnostic to rule out MI due to left circumflex occlusion. (*Level of Evidence: B*)
4. Continuous 12-lead ECG monitoring is a reasonable alternative to serial 12-lead recordings in patients whose initial ECG is nondiagnostic. (*Level of Evidence: B*)

#### *Class IIb*

1. For patients who present within 6 h of the onset of symptoms consistent with ACS, assessment of an early marker of cardiac injury (e.g., myoglobin) in conjunction with a late marker (e.g., troponin) may be considered. (*Level of Evidence: B*)
2. For patients who present within 6 h of symptoms suggestive of ACS, a 2-h delta creatine kinase myocardial band (CK-MB) mass in conjunction with 2-h delta troponin may be considered. (*Level of Evidence: B*)
3. For patients who present within 6 h of symptoms suggestive of ACS, myoglobin in conjunction with CK-MB mass or troponin when measured at baseline and 90 min may be considered. (*Level of Evidence: B*)
4. Measurement of B-type natriuretic peptide (BNP) or N-terminal pro-BNP (NT-pro-BNP) may be considered to supplement assessment of global risk in patients with suspected ACS. (*Level of Evidence: B*)

#### *Class III*

Total CK (without MB), aspartate aminotransferase (AST, SGOT), alanine transaminase, beta-hydroxybutyric dehydrogenase, and/or lactate dehydrogenase should not be utilized as primary tests for the detection of myocardial injury in patients with chest discomfort suggestive of ACS. (*Level of Evidence: C*)

**Table. Short-Term Risk of Death or Nonfatal MI in Patients With UA/NSTEMI\***

<b>Feature</b>	<b>High Risk</b>  <b><i>At least 1 of the following features must be present:</i></b>	<b>Intermediate Risk</b>  <b><i>No high-risk feature, but must have 1 or the following:</i></b>	<b>Low Risk</b>  <b><i>No high- or intermediate-risk feature but may have any of the following features:</i></b>
History	Accelerating tempo of ischemic symptoms in preceding 48 h	Prior MI, peripheral or cerebrovascular disease, or CABG; prior aspirin use	
Character of pain	Prolonged ongoing (greater than 20 min) rest pain	Prolonged (greater than 20 min) rest angina, now resolved, with moderate or high likelihood of CAD  Rest angina (greater	Increased angina frequency, severity, or duration  Angina provoked at a lower threshold

Feature	<b>High Risk</b>  <b><i>At least 1 of the following features must be present:</i></b>	<b>Intermediate Risk</b>  <b><i>No high-risk feature, but must have 1 or the following:</i></b>	<b>Low Risk</b>  <b><i>No high- or intermediate-risk feature but may have any of the following features:</i></b>
		<p>than 20 min) or relieved with rest or sublingual NTG</p> <p>Nocturnal angina</p> <p>New-onset or progressive Canadian Cardiovascular Society (CCS) class III or IV angina in the past 2 weeks without prolonged (greater than 20 min) rest pain but with intermediate or high likelihood of CAD (see Table 6 in the original document.)</p>	<p>New onset angina with onset 2 weeks to 2 months prior to presentation</p>
Clinical findings	<p>Pulmonary edema, most likely due to ischemia</p> <p>New or worsening mitral regurgitation (MR) murmur</p> <p>S<sub>3</sub> or new/worsening rales</p> <p>Hypotension, bradycardia, tachycardia</p> <p>Age greater than 75 years</p>	<p>Age greater than 70 years</p>	
ECG	<p>Angina at rest with transient ST-segment changes greater than 0.5 mm</p> <p>Bundle-branch block, new or presumed new</p> <p>Sustained ventricular tachycardia</p>	<p>T-wave changes</p> <p>Pathological Q waves or resting ST-depression less than 1 mm in multiple lead groups (anterior, inferior, lateral)</p>	<p>Normal or unchanged ECG</p>

<b>Feature</b>	<b>High Risk</b>  <b><i>At least 1 of the following features must be present:</i></b>	<b>Intermediate Risk</b>  <b><i>No high-risk feature, but must have 1 or the following:</i></b>	<b>Low Risk</b>  <b><i>No high- or intermediate-risk feature but may have any of the following features:</i></b>
Cardiac markers	Elevated cardiac troponin T (TnT), troponin I (TnI), or CK-MB (e.g., TnT or TnI greater than 0.1 ng per mL)	Slightly elevated cardiac TnT, TnI, or CK-MB (e.g., TnT greater than 0.01 but less than 0.1 ng per mL)	Normal
*Estimation of the short-term risks of death and nonfatal cardiac ischemic events in UA (or NSTEMI) is a complex multivariable problem that cannot be fully specified in a table such as this; therefore, this table is meant to offer general guidance and illustration rather than rigid algorithms.			

Adapted from AHCPR Clinical Practice Guidelines No. 10, Unstable Angina: Diagnosis and Management, May 1994 (124).

## **Immediate Management**

### *Class I*

1. The history, physical examination, 12-lead ECG, and initial cardiac biomarker tests should be integrated to assign patients with chest pain into 1 of 4 categories: a noncardiac diagnosis, chronic stable angina, possible ACS, and definite ACS. (*Level of Evidence: C*)
2. Patients with probable or possible ACS but whose initial 12-lead ECG and cardiac biomarker levels are normal should be observed in a facility with cardiac monitoring (e.g., chest pain unit or hospital telemetry ward), and repeat ECG (or continuous 12-lead ECG monitoring) and repeat cardiac biomarker measurement(s) should be obtained at predetermined, specified time intervals. (*Level of Evidence: B*)
3. In patients with suspected ACS in whom ischemic heart disease is present or suspected, if the follow-up 12-lead ECG and cardiac biomarkers measurements are normal, a stress test (exercise or pharmacological) to provoke ischemia should be performed in the ED, in a chest pain unit, or on an outpatient basis in a timely fashion (within 72 h) as an alternative to inpatient admission. Low-risk patients with a negative diagnostic test can be managed as outpatients. (*Level of Evidence: C*)
4. In low-risk patients who are referred for outpatient stress testing (see above), precautionary appropriate pharmacotherapy (e.g., ASA, sublingual NTG, and/or beta blockers) should be given while awaiting results of the stress test. (*Level of Evidence: C*)
5. Patients with definite ACS and ongoing ischemic symptoms, positive cardiac biomarkers, new ST-segment deviations, new deep T-wave inversions, hemodynamic abnormalities, or a positive stress test should be admitted to the hospital for further management. Admission to the critical care unit is recommended for those with active, ongoing ischemia/injury or hemodynamic or electrical instability. Otherwise, a telemetry step-down unit is reasonable. (*Level of Evidence: C*)

6. Patients with possible ACS and negative cardiac biomarkers who are unable to exercise or who have an abnormal resting ECG should undergo a pharmacological stress test. (*Level of Evidence: B*)
7. Patients with definite ACS and ST-segment elevation in leads V<sub>7</sub> to V<sub>9</sub> due to left circumflex occlusion should be evaluated for immediate reperfusion therapy. (*Level of Evidence: A*)
8. Patients discharged from the ED or chest pain unit should be given specific instructions for activity, medications, additional testing, and follow-up with a personal physician. (*Level of Evidence: C*)

### *Class IIa*

In patients with suspected ACS with a low or intermediate probability of CAD, in whom the follow-up 12-lead ECG and cardiac biomarkers measurements are normal, performance of a noninvasive coronary imaging test (i.e., coronary computed tomographic angiogram [CCTA]) is reasonable as an alternative to stress testing. (*Level of Evidence: B*)

### **Early Hospital Care**

**Table. Selection of Initial Treatment Strategy: Invasive Versus Conservative Strategy**

<b>Preferred Strategy</b>	<b>Patient Characteristics</b>
Invasive	Recurrent angina or ischemia at rest or with low-level activities despite intensive medical therapy  Elevated cardiac biomarkers (TnT or TnI)  New or presumably new ST-segment depression  Signs or symptoms of heart failure (HF) or new or worsening mitral regurgitation  High-risk findings from noninvasive testing  Hemodynamic instability  Sustained ventricular tachycardia  PCI within 6 months  Prior CABG  High risk score (e.g., TIMI, GRACE)  Reduced left ventricular function (left ventricular ejection fraction [LVEF] less than 40%)
Conservative	Low risk score (e.g., TIMI, GRACE)  Patient or physician preference in the absence of high-risk features

## Anti-Ischemic and Analgesic Therapy

### Class I

1. Bed/chair rest with continuous ECG monitoring is recommended for all UA/NSTEMI patients during the early hospital phase. (*Level of Evidence: C*)
2. Supplemental oxygen should be administered to patients with UA/NSTEMI with an arterial saturation less than 90%, respiratory distress, or other high-risk features for hypoxemia. (Pulse oximetry is useful for continuous measurement of arterial oxygen saturation [ $\text{SaO}_2$ ]) (*Level of Evidence: B*)
3. Patients with UA/NSTEMI with ongoing ischemic discomfort should receive sublingual NTG (0.4 mg) every 5 min for a total of 3 doses, after which assessment should be made about the need for intravenous NTG, if not contraindicated. (*Level of Evidence: C*)
4. Intravenous NTG is indicated in the first 48 h after UA/NSTEMI for treatment of persistent ischemia, HF, or hypertension. The decision to administer intravenous NTG and the dose used should not preclude therapy with other proven mortality-reducing interventions such as beta blockers or angiotensin-converting enzyme (ACE) inhibitors. (*Level of Evidence: B*)
5. Oral beta-blocker therapy should be initiated within the first 24 h for patients who do not have 1 or more of the following: 1) signs of HF, 2) evidence of a low-output state, 3) increased risk<sup>a</sup> for cardiogenic shock, or 4) other relative contraindications to beta blockade (PR interval greater than 0.24 s, second or third degree heart block, active asthma, or reactive airway disease). (*Level of Evidence: B*)
6. In UA/NSTEMI patients with continuing or frequently recurring ischemia and in whom beta blockers are contraindicated, a nondihydropyridine calcium channel blocker (e.g., verapamil or diltiazem) should be given as initial therapy in the absence of clinically significant left ventricular (LV) dysfunction or other contraindications. (*Level of Evidence: B*)
7. An ACE inhibitor should be administered orally within the first 24 h to UA/NSTEMI patients with pulmonary congestion or LVEF less than or equal to 0.40, in the absence of hypotension (systolic blood pressure less than 100 mm Hg or less than 30 mm Hg below baseline) or known contraindications to that class of medications. (*Level of Evidence: A*)
8. An angiotensin receptor blocker (ARB) should be administered to UA/NSTEMI patients who are intolerant of ACE inhibitors and have either clinical or radiological signs of HF or LVEF less than or equal to 0.40. (*Level of Evidence: A*)
9. Because of the increased risks of mortality, reinfarction, hypertension, HF, and myocardial rupture associated with their use, nonsteroidal anti-inflammatory drugs (NSAIDs), except for ASA, whether nonselective or cyclooxygenase (COX)-2-selective agents, should be discontinued at the time a patient presents with UA/NSTEMI. (*Level of Evidence: C*)

### Class IIa

1. It is reasonable to administer supplemental oxygen to all patients with UA/NSTEMI during the first 6 h after presentation. (*Level of Evidence: C*)
2. In the absence of contradictions to its use, it is reasonable to administer morphine sulfate intravenously to UA/NSTEMI patients if there is uncontrolled



- ischemic chest discomfort despite NTG, provided that additional therapy is used to manage the underlying ischemia. (*Level of Evidence: B*)
3. It is reasonable to administer intravenous (IV) beta blockers at the time of presentation for hypertension to UA/NSTEMI patients who do not have 1 or more of the following: 1) signs of HF, 2) evidence of low-output state, 3) increased risk<sup>a</sup> for cardiogenic shock, or 4) other relative contraindications to beta blockade (PR interval greater than 0.24 s, second or third degree heart block, active asthma, or reactive airway disease). (*Level of Evidence: B*)
  4. Oral long-acting nondihydropyridine calcium antagonists are reasonable for use in UA/NSTEMI patients for recurrent ischemia in the absence of contraindications after beta blockers and nitrates have been fully used. (*Level of Evidence: C*)
  5. An ACE inhibitor administered orally within the first 24 h of UA/NSTEMI can be useful in patients without pulmonary congestion or LVEF less than or equal to 0.40 in the absence of hypotension (systolic blood pressure less than 100 mm Hg or less than 30 mm Hg below baseline) or known contraindications to that class of medications. (*Level of Evidence: B*)
  6. Intra-aortic balloon pump (IABP) counterpulsation is reasonable in UA/NSTEMI patients for severe ischemia that is continuing or recurs frequently despite intensive medical therapy, for hemodynamic instability in patients before or after coronary angiography, and for mechanical complications of MI. (*Level of Evidence: C*)

#### *Class IIb*

1. The use of extended-release forms of nondihydropyridine calcium antagonists instead of a beta blocker may be considered in patients with UA/NSTEMI. (*Level of Evidence: B*)
2. Immediate-release dihydropyridine calcium antagonists in the presence of adequate beta blockade may be considered in patients with UA/NSTEMI with ongoing ischemic symptoms or hypertension. (*Level of Evidence: B*)

#### *Class III*

1. Nitrates should not be administered to UA/NSTEMI patients with systolic blood pressure less than 90 mm Hg or greater than or equal to 30 mm Hg below baseline, severe bradycardia (less than 50 beats per minute), tachycardia (more than 100 beats per minute) in the absence of symptomatic HF, or right ventricular infarction. (*Level of Evidence: C*)
2. Nitroglycerin or other nitrates should not be administered to patients with UA/NSTEMI who had received a phosphodiesterase inhibitor for erectile dysfunction within 24 h of sildenafil or 48 h of tadalafil use. The suitable time for the administration of nitrates after vardenafil has not been determined. (*Level of Evidence: C*)
3. Immediate-release dihydropyridine calcium antagonists should not be administered to patients with UA/NSTEMI in the absence of a beta blocker. (*Level of Evidence: A*)
4. An intravenous ACE inhibitor should not be given to patients within the first 24 h of UA/NSTEMI because of the increased risk of hypotension. (A possible exception may be patients with refractory hypertension.) (*Level of Evidence: B*)

5. It may be harmful to administer intravenous beta blockers to UA/NSTEMI patients who have contraindications to beta blockade, signs of HF or low-output state, or other risk factors<sup>a</sup> for cardiogenic shock. (*Level of Evidence: A*)
6. Nonsteroidal anti-inflammatory drugs (except for ASA), whether nonselective or COX-2-selective agents, should not be administered during hospitalization for UA/NSTEMI because of the increased risks of mortality, reinfarction, hypertension, HF, and myocardial rupture associated with their use. (*Level of Evidence: C*)

<sup>a</sup> Risk factors for cardiogenic shock (the greater the number of risk factors present, the higher the risk of developing cardiogenic shock): age greater than 70 years, systolic blood pressure less than 120 mmHg, sinus tachycardia greater than 110 or heart rate less than 60, increased time since onset of symptoms of UA/NSTEMI

## **Antiplatelet/Anticoagulant Therapy in Patients for Whom Diagnosis of US/NSTEMI is Likely or Definite**

### *Antiplatelet Therapy Recommendations*

#### *Class I*

1. Aspirin should be administered to UA/NSTEMI patients as soon as possible after hospital presentation and continued indefinitely in patients not known to be intolerant of that medication. (*Level of Evidence: A*) (See Figure 7 and 8; Box A in the original guideline document.)
2. Clopidogrel (loading dose followed by daily maintenance dose)<sup>b</sup> should be administered to UA/NSTEMI patients who are unable to take ASA because of hypersensitivity or major gastrointestinal intolerance. (*Level of Evidence: A*) (See Figure 7 and 8; Box A in the original guideline document.)
3. In UA/NSTEMI patients with a history of gastrointestinal bleeding, when ASA and clopidogrel are administered alone or in combination, drugs to minimize the risk of recurrent gastrointestinal bleeding (e.g., proton-pump inhibitors) should be prescribed concomitantly. (*Level of Evidence: B*)
4. For UA/NSTEMI patients in whom an initial invasive strategy is selected, antiplatelet therapy in addition to aspirin should be initiated before diagnostic angiography (upstream) with either clopidogrel (loading dose followed by daily maintenance dose)<sup>b</sup> or an intravenous glycoprotein (GP IIb/IIIa) inhibitor. (*Level of Evidence: A*) Abciximab as the choice for upstream GP IIb/IIIa therapy is indicated only if there is no appreciable delay to angiography and PCI is likely to be performed; otherwise, IV eptifibatide or tirofiban is the preferred choice of GP IIb/IIIa inhibitor. (*Level of Evidence: B*)
5. For UA/NSTEMI patients in whom an initial conservative (i.e., noninvasive) strategy is selected (See Section 3.3 in the original guideline document and "Initial Conservative Versus Initial Invasive Strategies" below.), clopidogrel (loading dose followed by daily maintenance dose)<sup>b</sup> should be added to ASA and anticoagulant therapy as soon as possible after admission and administered for at least 1 month (*Level of Evidence: A*) and ideally up to 1 year. (*Level of Evidence: B*) (See Figure 8; Box C2 in the original guideline document.)
6. For UA/NSTEMI patients in whom an initial conservative strategy is selected, if recurrent symptoms/ischemia, HF, or serious arrhythmias subsequently appear, then diagnostic angiography should be performed. (*Level of*

*Evidence: A*) (See Figure 8; Box D in the original guideline document.) Either an intravenous GP IIb/IIIa inhibitor (eptifibatide or tirofiban; *Level of Evidence: A*) or clopidogrel (loading dose followed by daily maintenance dose; *Level of Evidence: A*)<sup>b</sup> should be added to ASA and anticoagulant therapy before diagnostic angiography (upstream). (*Level of Evidence: C*)

### *Class IIa*

1. For UA/NSTEMI patients in whom an initial conservative strategy is selected and who have recurrent ischemic discomfort with clopidogrel, ASA, and anticoagulant therapy, it is reasonable to add a GP IIb/IIIa antagonist before diagnostic angiography. (*Level of Evidence: C*)
2. For UA/NSTEMI patients in whom an initial invasive strategy is selected, it is reasonable to initiate antiplatelet therapy with both clopidogrel (loading dose followed by daily maintenance dose)<sup>b</sup> and an intravenous GP IIb/IIIa inhibitor. (*Level of Evidence: B*) Abciximab as the choice for upstream GP IIb/IIIa therapy is indicated only if there is no appreciable delay to angiography and PCI is likely to be performed; otherwise, IV eptifibatide or tirofiban is the preferred choice of GP IIb/IIIa inhibitor.<sup>c</sup> (*Level of Evidence: B*)
3. For UA/NSTEMI patients in whom an initial invasive strategy is selected, it is reasonable to omit upstream administration of an intravenous GP IIb/IIIa antagonist before diagnostic angiography if bivalirudin is selected as the anticoagulant and at least 300 mg of clopidogrel was administered at least 6 h earlier than planned catheterization or PCI. (*Level of Evidence: B*)

### *Class IIb*

For UA/NSTEMI patients in whom an initial conservative (i.e., noninvasive) strategy is selected, it may be reasonable to add eptifibatide or tirofiban to anticoagulant and oral antiplatelet therapy. (*Level of Evidence: B*) (See Figure 8; Box C in the original guideline document.)

### *Class III*

Abciximab should not be administered to patients in whom PCI is not planned. (*Level of Evidence: A*)

<sup>b</sup> Some uncertainty exists about optimum dosing of clopidogrel. Randomized trials establishing its efficacy and providing data on bleeding risks used a loading dose of 300 mg orally followed by a daily oral maintenance dose of 75 mg. Higher oral loading doses such as 600 or 900 mg of clopidogrel more rapidly inhibit platelet aggregation and achieve a higher absolute level of inhibition of platelet aggregation, but the additive clinical efficacy and the safety of higher oral loading doses have not been rigorously established.

<sup>c</sup> Factors favoring administration of both clopidogrel and GP IIb/IIIa inhibitor include: delay to angiography, high-risk features, and early recurrent ischemic discomfort.

## *Anticoagulant Therapy Recommendations*

### *Class I*

Anticoagulant therapy should be added to antiplatelet therapy in UA/NSTEMI patients as soon as possible after presentation.

- a. For patients in whom an invasive strategy is selected, regimens with established efficacy at a *Level of Evidence: A* include enoxaparin and unfractionated heparin (UFH) (See Figure 7; Box B1 in the original guideline document), and those with established efficacy at a *Level of Evidence: B* include bivalirudin and fondaparinux (See Figure 7; Box B1 in the original guideline document)
- b. For patients in whom a conservative strategy is selected, regimens using either enoxaparin<sup>d</sup> or UFH (*Level of Evidence: A*) or fondaparinux (*Level of Evidence: B*) have established efficacy. (See Figure 8; Box C1 in the original guideline document)<sup>e</sup> See also Class IIa recommendation below.
- c. In patients in whom a conservative strategy is selected and who have an increased risk of bleeding, fondaparinux is preferable. (*Level of Evidence: B*) (See Figure 8; Box C1 in the original guideline document)

### *Class IIa*

For UA/NSTEMI patients in whom an initial conservative strategy is selected, enoxaparin<sup>d</sup> or fondaparinux is preferable to UFH as anticoagulant therapy, unless CABG is planned within 24 h. (*Level of Evidence: B*)

<sup>d</sup> Limited data are available for the use of other low molecular weight heparins (LMWHs) (e.g., dalteparin; See Tables 13 and 17 in the original guideline document) in UA/NSTEMI

### *Additional Management Considerations for Antiplatelet and Anticoagulant Therapy*

### *Class I*

1. For UA/NSTEMI patients in whom an initial conservative strategy is selected and no subsequent features appear that would necessitate diagnostic angiography (recurrent symptoms/ischemia, HF, or serious arrhythmias), a stress test should be performed. (*Level of Evidence: B*) See Figure 8; Box O in the original guideline document)
  - a. If, after stress testing, the patient is classified as not at low risk, diagnostic angiography should be performed. (*Level of Evidence: A*) (See Figure 8; Box E1 in the original guideline document)
  - b. If, after stress testing, the patient is classified as being at low risk (See Figure 8; Box E2 in the original guideline document)), the instructions noted below should be followed in preparation for discharge (See Figure 8; Box K in the original guideline document) (*Level of Evidence: A*):
    1. Continue ASA indefinitely. (*Level of Evidence: A*)
    2. Continue clopidogrel for at least 1 month (*Level of Evidence: A*) and ideally up to 1 year. (*Level of Evidence: B*)
    3. Discontinue intravenous GP IIb/IIIa inhibitor if started previously. (*Level of Evidence: A*)
    4. Continue UFH for 48 h or administer enoxaparin or fondaparinux for the duration of hospitalization, up to 8 d, and then discontinue anticoagulant therapy. (*Level of Evidence: A*)
2. For UA/NSTEMI patients in whom CABG is selected as a postangiography management strategy, the instructions noted below should be followed (See Figure 9; Box G in the original guideline document).

- a. Continue ASA. (*Level of Evidence: A*)
- b. Discontinue clopidogrel 5 to 7 d before elective coronary artery bypass graft surgery, (CABG). (*Level of Evidence: B*) More urgent surgery, if necessary, may be performed by experienced surgeons if the incremental bleeding risk is considered acceptable. (*Level of Evidence: C*)
- c. Discontinue intravenous GP IIb/IIIa inhibitor (eptifibatide or tirofiban) 4 h before CABG. (*Level of Evidence: B*)
- d. Anticoagulant therapy should be managed as follows:
  1. Continue UFH. (*Level of Evidence: B*)
  2. Discontinue enoxaparin<sup>e</sup> 12 to 24 h before CABG and dose with UFH per institutional practice. (*Level of Evidence: B*)
  3. Discontinue fondaparinux 24 h before CABG and dose with UFH per institutional practice. (*Level of Evidence: B*)
  4. Discontinue bivalirudin 3 h before CABG and dose with UFH per institutional practice. (*Level of Evidence: B*)

<sup>e</sup> Limited data are available for the use of other LMWHs (e.g., dalteparin; see Figure 9; Box J in the original guideline document) in UA/NSTEMI.

3. For UA/NSTEMI patients in whom PCI has been selected as a postangiography management strategy, the instructions noted below should be followed (See Figure 9; Box H in the original guideline document):
  - a. Continue ASA. (*Level of Evidence: A*)
  - b. Administer a loading dose of clopidogrel<sup>f</sup> if not started before diagnostic angiography. (*Level of Evidence: A*)
  - c. Administer an intravenous GP IIb/IIIa inhibitor (abciximab, eptifibatide, or tirofiban) if not started before diagnostic angiography for troponin-positive and other high-risk patients (*Level of Evidence: A*). See Class IIa recommendation below if bivalirudin was selected as the anticoagulant.
  - d. Discontinue anticoagulant therapy after PCI for uncomplicated cases. (*Level of Evidence: B*)
4. For UA/NSTEMI patients in whom medical therapy is selected as a postangiography management strategy and in whom no significant obstructive CAD on angiography was found, antiplatelet and anticoagulant therapy should be administered at the discretion of the clinician. (*Level of Evidence: C*) For patients in whom evidence of coronary atherosclerosis is present (e.g., luminal irregularities or intravascular ultrasound-demonstrated lesions), albeit without flow-limiting stenoses, long-term treatment with ASA and other secondary prevention measures should be prescribed. (See Figure 9; Box I in the original guideline document) (*Level of Evidence: C*)
5. For UA/NSTEMI patients in whom medical therapy is selected as a postangiography management strategy and in whom CAD was found on angiography, the following approach is recommended (See Figure 9; Box J in the original guideline document):
  - a. Continue ASA. (*Level of Evidence: A*)
  - b. Administer a loading dose of clopidogrel<sup>f</sup> if not given before diagnostic angiography. (*Level of Evidence: A*)
  - c. Discontinue intravenous GP IIb/IIIa inhibitor if started previously. (*Level of Evidence: B*)
  - d. Anticoagulant therapy should be managed as follows:

1. Continue intravenous UFH for at least 48 h or until discharge if given before diagnostic angiography. (*Level of Evidence: A*)
2. Continue enoxaparin for duration of hospitalization, up to 8 d, if given before diagnostic angiography. (*Level of Evidence: A*)
3. Continue fondaparinux for duration of hospitalization, up to 8 d, if given before diagnostic angiography. (*Level of Evidence: B*)
4. Either discontinue bivalirudin or continue at a dose of 0.25 mg per kg per h for up to 72 h at the physician's discretion, if given before diagnostic angiography. (*Level of Evidence: B*)

<sup>f</sup> Some uncertainty exists about optimum dosing of clopidogrel. Randomized trials establishing its efficacy and providing data on bleeding risks used a loading dose of 300 mg orally followed by a daily oral maintenance dose of 75 mg. Higher oral loading doses such as 600 or 900 mg of clopidogrel more rapidly inhibit platelet aggregation and achieve a higher absolute level of inhibition of platelet aggregation, but the additive clinical efficacy and the safety of higher oral loading doses have not been rigorously established.

6. For UA/NSTEMI patients in whom a conservative strategy is selected and who do not undergo angiography or stress testing, the instructions noted below should be followed (See Figure 8; Box K in the original guideline document):
  - a. Continue ASA indefinitely. (*Level of Evidence: A*)
  - b. Continue clopidogrel for at least 1 month (*Level of Evidence: A*) and ideally up to 1 year. (*Level of Evidence: B*)
  - c. Discontinue IV GP IIb/IIIa inhibitor if started previously. (*Level of Evidence: A*)
  - d. Continue UFH for 48 h or administer enoxaparin or fondaparinux for the duration of hospitalization, up to 8 d, and then discontinue anticoagulant therapy. (*Level of Evidence: A*)
7. For UA/NSTEMI patients in whom an initial conservative strategy is selected and in whom no subsequent features appear that would necessitate diagnostic angiography (recurrent symptoms/ischemia, HF, or serious arrhythmias), LVEF should be measured. (*Level of Evidence: B*) (See Figure 8; Box L in the original guideline document.)

#### *Class IIa*

1. For UA/NSTEMI patients in whom PCI is selected as a postangiography management strategy, it is reasonable to omit administration of an intravenous GP IIb/IIIa antagonist if bivalirudin was selected as the anticoagulant and at least 300 mg of clopidogrel was administered at least 6 h earlier. (*Level of Evidence: B*) (See Figure 9; in the original guideline document.)
2. If LVEF is less than or equal to 0.40, it is reasonable to perform diagnostic angiography. (*Level of Evidence: B*) (See Figure 8; Box M in the original guideline document.)
3. If LVEF is greater than 0.40, it is reasonable to perform a stress test. (*Level of Evidence: B*) (See Figure 8; Box N in the original guideline document.)

#### *Class IIb*

For UA/NSTEMI patients in whom PCI is selected as a postangiography management strategy, it may be reasonable to omit an intravenous GP IIb/IIIa

inhibitor if not started before diagnostic angiography for troponin-negative patients without other clinical or angiographic high-risk features. (*Level of Evidence: C*)

### *Class III*

Intravenous fibrinolytic therapy is not indicated in patients without acute ST-segment elevation, a true posterior MI, or a presumed new left bundle-branch block. (*Level of Evidence: A*)

## **Initial Conservative Versus Initial Invasive Strategies**

### *Class I*

1. An early invasive strategy (i.e., diagnostic angiography with intent to perform revascularization) is indicated in UA/NSTEMI patients who have refractory angina or hemodynamic or electrical instability (without serious comorbidities or contraindications to such procedures). (*Level of Evidence: B*)
2. An early invasive strategy (i.e., diagnostic angiography with intent to perform revascularization) is indicated in initially stabilized UA/NSTEMI patients (without serious comorbidities or contraindications to such procedures) who have an elevated risk for clinical events (See Table below: and Sections 2.2.6 and 3.4.3 in the original guideline document). (*Level of Evidence: A*)

### *Class IIb*

1. In initially stabilized patients, an initially conservative (i.e., a selectively invasive) strategy may be considered as a treatment strategy for UA/NSTEMI patients (without serious comorbidities or contraindications to such procedures) who have an elevated risk for clinical events (See Table below and Sections 2.2.6 and 3.4.3 in the original guideline document) including those who are troponin positive. (*Level of Evidence: B*) The decision to implement an initial conservative (vs. initial invasive) strategy in these patients may consider physician and patient preference. (*Level of Evidence: C*)
2. An invasive strategy may be reasonable in patients with chronic renal insufficiency. (*Level of Evidence: C*)

### *Class III*

1. An early invasive strategy (i.e., diagnostic angiography with intent to perform revascularization) is not recommended in patients with extensive comorbidities (e.g., liver or pulmonary failure, cancer), in whom the risks of revascularization and comorbid conditions are likely to outweigh the benefits of revascularization. (*Level of Evidence: C*)
2. An early invasive strategy (i.e., diagnostic angiography with intent to perform revascularization) is not recommended in patients with acute chest pain and a low likelihood of ACS. (*Level of Evidence: C*)
3. An early invasive strategy (i.e., diagnostic angiography with intent to perform revascularization) should not be performed in patients who will not consent to revascularization regardless of the findings. (*Level of Evidence: C*)

**Table. Selection of Initial Treatment Strategy: Invasive Versus Conservative Strategy**

Preferred Strategy	Patient Characteristics
Invasive	<p>Recurrent angina or ischemia at rest or with low-level activities despite intensive medical therapy</p> <p>Elevated cardiac biomarkers (TnT or TnI)</p> <p>New or presumably new ST-segment depression</p> <p>Signs or symptoms of HF or new or worsening mitral regurgitation</p> <p>High-risk findings from noninvasive testing</p> <p>Hemodynamic instability</p> <p>Sustained ventricular tachycardia</p> <p>PCI within 6 months</p> <p>Prior CABG</p> <p>High risk score (e.g., TIMI, GRACE)</p> <p>Reduced left ventricular function (LVEF less than 40%)</p>
Conservative	<p>Low risk score (e.g., TIMI, GRACE)</p> <p>Patient or physician preference in the absence of high-risk features</p>

### **Risk Stratification Before Discharge**

#### *Class I*

1. Noninvasive stress testing is recommended in low-risk patients (See Table above: Short-Term Risk of Death or Nonfatal MI in Patients With UA/NSTEMI) who have been free of ischemia at rest or with low-level activity and of HF for a minimum of 12 to 24 h. (*Level of Evidence: C*)
2. Noninvasive stress testing is recommended in patients at intermediate risk (See Table above: Short-Term Risk of Death or Nonfatal MI in Patients With UA/NSTEMI) who have been free of ischemia at rest or with low-level activity and of HF for a minimum of 12 to 24 h. (*Level of Evidence: C*)
3. Choice of stress test is based on the resting ECG, ability to perform exercise, local expertise, and technologies available. Treadmill exercise is useful in patients able to exercise in whom the ECG is free of baseline ST-segment abnormalities, bundle-branch block, LV hypertrophy, intraventricular conduction defect, paced rhythm, preexcitation, and digoxin effect. (*Level of Evidence: C*)
4. An imaging modality should be added in patients with resting ST-segment depression (greater than or equal to 0.10 mV), LV hypertrophy, bundle-branch block, intraventricular conduction defect, preexcitation, or digoxin who



- are able to exercise. In patients undergoing a low-level exercise test, an imaging modality can add sensitivity. (*Level of Evidence: B*)
5. Pharmacological stress testing with imaging is recommended when physical limitations (e.g., arthritis, amputation, severe peripheral vascular disease, severe chronic obstructive pulmonary disease, or general debility) preclude adequate exercise stress. (*Level of Evidence: B*)
  6. Prompt angiography without noninvasive risk stratification should be performed for failure of stabilization with intensive medical treatment. (*Level of Evidence: B*)
  7. A noninvasive test (echocardiogram or radionuclide angiogram) is recommended to evaluate LV function in patients with definite ACS who are not scheduled for coronary angiography and left ventriculography. (*Level of Evidence: B*)

### **Coronary Revascularization**

#### **Recommendations for Revascularization With PCI and CABG in Patients With UA/NSTEMI**

(See Figure 20 in the original guideline document for details of the decision tree.)

##### *Recommendations for PCI*

##### *Class I*

1. An early invasive PCI strategy is indicated for patients with UA/NSTEMI who have no serious comorbidity and who have coronary lesions amenable to PCI and any of the high-risk features listed in section 3.3 in the original guideline document for details of the decision tree. (See Section 3.3 and "Initial Conservative Versus Initial Invasive Strategies" above for specific recommendations and their Level of Evidence.)
2. Percutaneous coronary intervention (or CABG) is recommended for UA/NSTEMI patients with 1- or 2-vessel CAD with or without significant proximal left anterior descending CAD but with a large area of viable myocardium and high-risk criteria on noninvasive testing. (*Level of Evidence: B*)
3. Percutaneous coronary intervention (or CABG) is recommended for UA/NSTEMI patients with multivessel coronary disease with suitable coronary anatomy, with normal LV function, and without diabetes mellitus. (*Level of Evidence: A*)
4. An intravenous platelet GP IIb/IIIa inhibitor is generally recommended in UA/NSTEMI patients undergoing PCI. (*Level of Evidence: A*) See Section 3.2.3 and Figures 7, 8, and 9 in the original document for details on timing and dosing recommendations (See Table 13 in the original guideline document)

##### *Class IIa*

1. Percutaneous coronary intervention is reasonable for focal saphenous vein graft (SVG) lesions or multiple stenoses in UA/NSTEMI patients who are undergoing medical therapy and who are poor candidates for reoperative surgery. (*Level of Evidence: C*)

2. Percutaneous coronary intervention (or CABG) is reasonable for UA/NSTEMI patients with 1- or 2-vessel CAD with or without significant proximal left anterior descending CAD but with a moderate area of viable myocardium and ischemia on noninvasive testing. (*Level of Evidence: B*)
3. Percutaneous coronary intervention (or CABG) can be beneficial compared with medical therapy for UA/NSTEMI patients with 1-vessel disease with significant proximal left anterior descending CAD. (*Level of Evidence: B*)
4. Use of PCI is reasonable in patients with UA/NSTEMI with significant left main CAD (greater than 50% diameter stenosis) who are candidates for revascularization but are not eligible for CABG or who require emergent intervention at angiography for hemodynamic instability. (*Level of Evidence: B*)

#### *Class IIb*

1. In the absence of high-risk features associated with UA/NSTEMI, PCI may be considered in patients with single-vessel or multi vessel CAD who are undergoing medical therapy and who have 1 or more lesions to be dilated with a reduced likelihood of success. (*Level of Evidence: B*)
2. Percutaneous coronary intervention may be considered for UA/NSTEMI patients who are undergoing medical therapy who have 2- or 3-vessel disease, significant proximal left anterior descending CAD, and treated diabetes or abnormal LV function, with anatomy suitable for catheter-based therapy. (*Level of Evidence: B*)

#### *Class III*

1. Percutaneous coronary intervention (or CABG) is not recommended for patients with 1- or 2-vessel CAD without significant proximal left anterior descending CAD with no current symptoms or symptoms that are unlikely to be due to myocardial ischemia and who have no ischemia on noninvasive testing. (*Level of Evidence: C*)
2. In the absence of high-risk features associated with UA/NSTEMI, PCI is not recommended for patients with UA/NSTEMI who have single-vessel or multivessel CAD and no trial of medical therapy, or who have 1 or more of the following:
  - a. Only a small area of myocardium at risk. (*Level of Evidence: C*)
  - b. All lesions or the culprit lesion to be dilated with morphology that conveys a low likelihood of success. (*Level of Evidence: C*)
  - c. A high risk of procedure-related morbidity or mortality. (*Level of Evidence: C*)
  - d. Insignificant disease (less than 50% coronary stenosis). (*Level of Evidence: C*)
  - e. Significant left main CAD and candidacy for CABG. (*Level of Evidence: B*)
3. A PCI strategy in stable patients with persistently occluded infarct-related coronary arteries after NSTEMI is not indicated. (*Level of Evidence: B*)

#### *Recommendations for CABG*

#### *Class I*

1. Coronary artery bypass graft surgery is recommended for UA/NSTEMI patients with significant left main CAD (greater than 50% stenosis). (*Level of Evidence: A*)
2. Coronary artery bypass graft surgery is recommended for UA/NSTEMI patients with 3-vessel disease; the survival benefit is greater in patients with abnormal LV function (LVEF less than 0.50). (*Level of Evidence: A*)
3. Coronary artery bypass graft surgery is recommended for UA/NSTEMI patients with 2-vessel disease with significant proximal left anterior descending CAD and either abnormal LV function (LVEF less than 0.50) or ischemia on noninvasive testing. (*Level of Evidence: A*)
4. Coronary artery bypass graft surgery is recommended for UA/NSTEMI patients in whom percutaneous revascularization is not optimal or possible and who have ongoing ischemia not responsive to maximal nonsurgical therapy. (*Level of Evidence: B*)
5. Coronary artery bypass graft surgery (or PCI) is recommended for UA/NSTEMI patients with 1- or 2-vessel CAD with or without significant proximal left anterior descending CAD but with a large area of viable myocardium and high-risk criteria on noninvasive testing. (*Level of Evidence: B*)
6. Coronary artery bypass graft surgery (or PCI) is recommended for UA/NSTEMI patients with multivessel coronary disease with suitable coronary anatomy, with normal LV function, and without diabetes mellitus. (*Level of Evidence: A*)

#### *Class IIa*

1. For patients with UA/NSTEMI and multivessel disease, CABG with use of the internal mammary arteries can be beneficial over PCI in patients being treated for diabetes. (*Level of Evidence: B*)
2. It is reasonable to perform CABG with the internal mammary artery for UA/NSTEMI patients with multivessel disease and treated diabetes mellitus. (*Level of Evidence: B*)
3. Repeat CABG is reasonable for UA/NSTEMI patients with multiple SVG stenoses, especially when there is significant stenosis of a graft that supplies the left anterior descending coronary artery (LAD). (*Level of Evidence: C*)
4. Coronary artery bypass graft surgery (or PCI) is reasonable for UA/NSTEMI patients with 1- or 2-vessel CAD with or without significant proximal left anterior descending CAD but with a moderate area of viable myocardium and ischemia on noninvasive testing. (*Level of Evidence: B*)
5. Coronary artery bypass graft surgery (or PCI) can be beneficial compared with medical therapy for UA/NSTEMI patients with 1-vessel disease with significant proximal left anterior descending CAD. (*Level of Evidence: B*)
6. Coronary artery bypass graft surgery (or PCI with stenting) is reasonable for patients with multivessel disease and symptomatic myocardial ischemia. (*Level of Evidence: B*)

#### *Class IIb*

Coronary artery bypass graft surgery may be considered in patients with UA/NSTEMI who have 1- or 2-vessel disease not involving the proximal LAD with a modest area of ischemic myocardium when percutaneous revascularization is not optimal or possible. (If there is a large area of viable myocardium and high-

risk criteria on noninvasive testing, this recommendation becomes a Class I recommendation.) (*Level of Evidence: B*)

### *Class III*

Coronary artery bypass graft surgery (or PCI) is not recommended for patients with 1- or 2-vessel CAD without significant proximal left anterior descending CAD with no current symptoms or symptoms that are unlikely to be due to myocardial ischemia and who have no ischemia on noninvasive testing. (*Level of Evidence: C*)

## **Late Hospital Care, Hospital Discharge, and Post-Hospital Discharge Care**

### **Medical Regimen and Use of Medications**

#### *Class I*

1. Medications required in the hospital to control ischemia should be continued after hospital discharge in patients with UA/NSTEMI who do not undergo coronary revascularization, patients with unsuccessful revascularization, and patients with recurrent symptoms after revascularization. Upward or downward titration of the doses may be required. (*Level of Evidence: C*)
2. All post-UA/NSTEMI patients should be given sublingual or spray NTG and instructed in its use. (*Level of Evidence: C*)
3. Before hospital discharge, patients with UA/NSTEMI should be informed about symptoms of worsening myocardial ischemia and MI and should be instructed in how and when to seek emergency care and assistance if such symptoms occur. (*Level of Evidence: C*)
4. Before hospital discharge, post-UA/NSTEMI patients and/or designated responsible caregivers should be provided with supportable, easily understood, and culturally sensitive instructions with respect to medication type, purpose, dose, frequency, and pertinent side effects. (*Level of Evidence: C*)
5. In post-UA/NSTEMI patients, anginal discomfort lasting more than 2 or 3 min should prompt the patient to discontinue physical activity or remove himself or herself from any stressful event. If pain does not subside immediately, the patient should be instructed to take 1 dose of NTG sublingually. If the chest discomfort/pain is unimproved or worsening 5 min after 1 NTG dose has been taken, it is recommended that the patient or a family member/friend call 9-1-1 immediately to access EMS. While activating EMS access, additional NTG (at 5-min intervals 2 times) may be taken while lying down or sitting. (*Level of Evidence: C*)
6. If the pattern or severity of anginal symptoms changes, which suggests worsening myocardial ischemia (e.g., pain is more frequent or severe or is precipitated by less effort or now occurs at rest), the patient should contact his or her physician without delay to assess the need for additional treatment or testing. (*Level of Evidence: C*)

### **Long-Term Medical Therapy and Secondary Prevention**

#### *Antiplatelet Therapy*

See Figure 11 in the original guideline document for antiplatelet therapy recommendations in algorithm format.

### *Class I*

1. For UA/NSTEMI patients treated medically without stenting, aspirin<sup>g</sup> (75 to 162 mg per day) should be prescribed indefinitely (*Level of Evidence: A*); clopidogrel<sup>h</sup> (75 mg per day) should be prescribed for at least 1 month (*Level of Evidence: A*) and ideally up to 1 year. (*Level of Evidence: B*)
2. For UA/NSTEMI patients treated with bare-metal stents, aspirin<sup>g</sup> 162 to 325 mg per day should be prescribed for at least 1 month (*Level of Evidence: B*), then continued indefinitely at a dose of 75 to 162 mg per day (*Level of Evidence: A*); clopidogrel should be prescribed at a dose of 75 mg per day for a minimum of 1 month and ideally for up to 1 year (unless the patient is at increased risk of bleeding; then it should be given for a minimum of 2 weeks). (*Level of Evidence: B*)
3. For UA/NSTEMI patients treated with drug-eluting stent (DES), aspirin<sup>g</sup> 162 to 325 mg per day should be prescribed for at least 3 months after sirolimus-eluting stent implantation and 6 months after paclitaxel-eluting stent implantation then continued indefinitely at a dose of 75 to 162 mg per day. (*Level of Evidence: B*) Clopidogrel 75 mg daily should be given for at least 12 months to all post-PCI patients receiving DES. (*Level of Evidence: B*)
4. Clopidogrel 75 mg daily (preferred) or ticlopidine (in the absence of contraindications) should be given to patients recovering from UA/NSTEMI when ASA is contraindicated or not tolerated because of hypersensitivity or gastrointestinal intolerance (but with gastroprotective agents such as proton-pump inhibitors). (*Level of Evidence: A*)

### *Class IIa*

For UA/NSTEMI patients in whom the physician is concerned about the risk of bleeding, a lower initial aspirin dose after PCI of 75 to 162 mg per day is reasonable. (*Level of Evidence: C*)

### *Class IIb*

For UA/NSTEMI patients who have an indication for anticoagulation, add warfarin<sup>i</sup> to maintain an international normalization ratio (INR) of 2.0 to 3.0.<sup>j</sup> (*Level of Evidence: B*)

### *Class III*

Dipyridamole is not recommended as an antiplatelet agent in post-UA/NSTEMI patients because it has not been shown to be effective. (*Level of Evidence: A*)

<sup>g</sup> For ASA-allergic patients, use clopidogrel alone (indefinitely), or try aspirin desensitization.

<sup>h</sup> For clopidogrel-allergic patients, use ticlopidine 250 mg by mouth twice daily.

<sup>i</sup> Continue ASA indefinitely and warfarin longer term as indicated for specific conditions such as atrial fibrillation; LV thrombus; or cerebral, venous, or pulmonary emboli

<sup>j</sup> An INR of 2.0 to 2.5 is preferable while given with ASA and clopidogrel, especially in older patients and those with other risk factors for bleeding

## *Beta Blockers*

### *Class I*

1. Beta blockers are indicated for all patients recovering from UA/NSTEMI unless contraindicated. (For those at low risk, see Class IIa recommendation below). Treatment should begin within a few days of the event, if not initiated acutely, and should be continued indefinitely. (*Level of Evidence: B*)
2. Patients recovering from UA/NSTEMI with moderate or severe LV failure should receive beta-blocker therapy with a gradual titration scheme. (*Level of Evidence: B*)

### *Class IIa*

It is reasonable to prescribe beta blockers to low-risk patients (i.e., normal LV function, revascularized, no high-risk features) recovering from UA/NSTEMI in the absence of absolute contraindications. (*Level of Evidence: B*)

## *Inhibition of the Renin-Angiotensin-Aldosterone System*

### *Class I*

1. Angiotensin-converting enzyme inhibitors should be given and continued indefinitely for patients recovering from UA/NSTEMI with HF, LV dysfunction (LVEF less than 0.40), hypertension, or diabetes mellitus, unless contraindicated. (*Level of Evidence: A*)
2. An angiotensin receptor blocker should be prescribed at discharge to those UA/NSTEMI patients who are intolerant of an ACE inhibitor and who have either clinical or radiological signs of HF and LVEF less than 0.40. (*Level of Evidence: A*)
3. Long-term aldosterone receptor blockade should be prescribed for UA/NSTEMI patients without significant renal dysfunction (estimated creatinine clearance should be greater than 30 mL per min) or hyperkalemia (potassium should be less than or equal to 5 mEq per liter) who are already receiving therapeutic doses of an ACE inhibitor, have an LVEF less than or equal to 0.40, and have either symptomatic HF or diabetes mellitus. (*Level of Evidence: A*)

### *Class IIa*

1. Angiotensin-converting enzyme inhibitors are reasonable for patients recovering from UA/NSTEMI in the absence of LV dysfunction, hypertension, or diabetes mellitus unless contraindicated. (*Level of Evidence: A*)
2. Angiotensin-converting enzyme inhibitors are reasonable for patients with HF and LVEF greater than 0.40. (*Level of Evidence: A*)
3. In UA/NSTEMI patients who do not tolerate ACE inhibitors, an angiotensin receptor blocker can be useful as an alternative to ACE inhibitors in long-term management provided there are either clinical or radiological signs of HF and LVEF less than 0.40. (*Level of Evidence: B*)

### *Class IIb*

The combination of an ACE inhibitor and an angiotensin receptor blocker may be considered in the long-term management of patients recovering from UA/NSTEMI with persistent symptomatic HF and LVEF less than 0.40<sup>k</sup> despite conventional therapy including an ACE inhibitor or an angiotensin receptor blocker alone. (*Level of Evidence: B*)

<sup>k</sup> The safety of this combination has not been proven in patients also on aldosterone antagonist and is not recommended.

### *Nitroglycerin*

#### *Class I*

Nitroglycerin to treat ischemic symptoms is recommended. (*Level of Evidence: C*)

### *Calcium Channel Blockers*

#### *Class I*

1. Calcium channel blockers<sup>l</sup> are recommended for ischemic symptoms when beta blockers are not successful. (*Level of Evidence: B*)
2. Calcium channel blockers<sup>l</sup> are recommended for ischemic symptoms when beta blockers are contraindicated or cause unacceptable side effects. (*Level of Evidence: C*)

<sup>l</sup> Short-acting dihydropyridine calcium channel antagonists should be avoided.

### *Warfarin Therapy*

#### *Class I*

Use of warfarin in conjunction with ASA and/or clopidogrel is associated with an increased risk of bleeding and should be monitored closely. (*Level of Evidence: A*)

### *Class IIb*

Warfarin either without (INR 2.5 to 3.5) or with low-dose ASA (75 to 81 mg per d; INR 2.0 to 2.5) may be reasonable for patients at high CAD risk and low bleeding risk who do not require or are intolerant of clopidogrel. (*Level of Evidence: B*)

### *Lipid Management*

#### *Class I*

1. The following lipid recommendations are beneficial:
  - a. Lipid management should include assessment of a fasting lipid profile for all patients, within 24 h of hospitalization. (*Level of Evidence: C*)
  - b. Hydroxymethyl glutaryl-coenzyme A reductase inhibitors (statins), in the absence of contraindications, regardless of baseline LDL-C and diet

- modification, should be given to post-UA/NSTEMI patients, including postrevascularization patients. (*Level of Evidence: A*)
- c. For hospitalized patients, lipid-lowering medications should be initiated before discharge. (*Level of Evidence: A*)
  - d. For UA/NSTEMI patients with elevated Low-density lipoprotein cholesterol (LDL-C) (greater than or equal to 100 mg per dL), cholesterol-lowering therapy should be initiated or intensified to achieve an LDL-C of less than 100 mg per dL. (*Level of Evidence: A*) Further titration to less than 70 mg per dL is reasonable. (*Class IIa, Level of Evidence: A*)
  - e. Therapeutic options to reduce non-high-density lipoprotein cholesterol (HDL-C)<sup>m</sup> are recommended, including more intense LDL-C-lowering therapy. (*Level of Evidence: B*)
  - f. Dietary therapy for all patients should include reduced intake of saturated fats (to less than 7% of total calories), cholesterol (to less than 200 mg per d), and trans fat (to less than 1% of energy). (*Level of Evidence: B*)
  - g. Promoting daily physical activity and weight management are recommended. (*Level of Evidence: B*)
2. Treatment of triglycerides and non-HDL-C is useful, including the following:
    - a. If triglycerides are 200 to 499 mg per dL, non-HDL-C<sup>m</sup> should be less than 130 mg per dL. (*Level of Evidence: B*)
    - b. If triglycerides are greater than or equal to 500 mg per dL<sup>n</sup>, therapeutic options to prevent pancreatitis are fibrate<sup>o</sup> or niacin<sup>o</sup> before LDL-lowering therapy is recommended. It is also recommended that LDL-C be treated to goal after triglyceride-lowering therapy. Achievement of a non-HDL-C<sup>m</sup> less than 130 mg per dL (i.e., 30 mg per dL greater than LDL-C target) if possible is recommended. (*Level of Evidence: C*)

### *Class IIa*

1. The following lipid management strategies can be beneficial:
  - a. Further reduction of LDL-C to less than 70 mg per dL is reasonable. (*Level of Evidence: A*)
  - b. If baseline LDL cholesterol is 70 to 100 mg per dL, it is reasonable to treat LDL-C to less than 70 mg per dL. (*Level of Evidence: B*)
  - c. Further reduction of non-HDL-C<sup>m</sup> to less than 100 mg per dL is reasonable; if triglycerides are 200 to 499 mg per dL, non-HDL-C target is less than 130 mg per dL. (*Level of Evidence: B*)
  - d. Therapeutic options to reduce non-HDL-C<sup>m</sup> (after LDL-C lowering) include niacin<sup>o</sup> or fibrate<sup>n</sup> therapy.
  - e. Nicotinic acid (niacin)<sup>o</sup> and fibric acid derivatives (fenofibrate, gemfibrozil)<sup>n</sup> can be useful as therapeutic options (after LDL-C-lowering therapy) for HDL-C less than 40 mg per dL. (*Level of Evidence: B*)
  - f. Nicotinic acid (niacin)<sup>o</sup> and fibric acid derivatives (fenofibrate, gemfibrozil)<sup>n</sup> can be useful as therapeutic options (after LDL-C-lowering therapy) for triglycerides greater than 200 mg per dL. (*Level of Evidence: B*)



- g. The addition of plant stanol/sterols (2 g per d) and viscous fiber (more than 10 g per d) is reasonable to further lower LDL-C. (*Level of Evidence: A*)

### *Class IIb*

Encouraging consumption of omega-3 fatty acids in the form of fish<sup>p</sup> or in capsule form (1 g per d) for risk reduction may be reasonable. For treatment of elevated triglycerides, higher doses (2 to 4 g per d) may be used for risk reduction. (*Level of Evidence: B*)

<sup>m</sup> Non-HDL-C = total cholesterol minus HDL-C

<sup>n</sup> Patients with very high triglycerides should not consume alcohol. The use of bile acid sequestrants is relatively contraindicated when triglycerides are greater than 200 mg per dL.

<sup>o</sup> The combination of high-dose statin plus fibrate can increase risk for severe myopathy. Statin doses should be kept relatively low with this combination. Dietary supplement niacin must not be used as a substitute for prescription niacin.

<sup>p</sup> Pregnant and lactating women should limit their intake of fish to minimize exposure to methylmercury.

### *Blood Pressure Control*

#### *Class I*

Blood pressure control according to Joint National Committee (JNC 7) guidelines<sup>q</sup> is recommended (i.e., blood pressure less than 140/90 mm Hg or less than 130/80 mm Hg if the patient has diabetes mellitus or chronic kidney disease). (*Level of Evidence: A*) Additional measures recommended to treat and control blood pressure include the following:

- a. Patients should initiate and/or maintain lifestyle modifications, including weight control, increased physical activity, alcohol moderation, sodium reduction, and emphasis on increased consumption of fresh fruits, vegetables, and low-fat dairy products. (*Level of Evidence: B*)
- b. For patients with blood pressure greater than or equal to 140/90 mm Hg (or greater than or equal to 130/80 mm Hg for individuals with chronic kidney disease or diabetes mellitus), it is useful to add blood pressure medication as tolerated, treating initially with beta blockers and/or ACE inhibitors, with addition of other drugs such as thiazides as needed to achieve target blood pressure. (*Level of Evidence: A*)

<sup>q</sup> Chobanian AV, Bakris GL, Black HR, et al., for the National High Blood Pressure Education Program Coordinating Committee. The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; the JNC 7 report. JAMA 2003;289:2560-72 (656).

### *Diabetes Mellitus*

#### *Class I*

Diabetes management should include lifestyle and pharmacotherapy measures to achieve a near-normal glycated hemoglobin (HbA1c) level of less than 7%. (*Level of Evidence: B*) Diabetes management should also include the following:

- a. Vigorous modification of other risk factors (e.g., physical activity, weight management, blood pressure control, and cholesterol management) as recommended should be initiated and maintained. (*Level of Evidence: B*)
- b. It is useful to coordinate the patient's diabetic care with the patient's primary care physician or endocrinologist. (*Level of Evidence: C*)

### *Smoking Cessation*

#### *Class I*

Smoking cessation and avoidance of exposure to environmental tobacco smoke at work and home are recommended. Follow-up, referral to special programs, or pharmacotherapy (including nicotine replacement) is useful, as is adopting a stepwise strategy aimed at smoking cessation (the 5 As are: Ask, Advise, Assess, Assist, and Arrange). (*Level of Evidence: B*)

### *Weight Management*

#### *Class I*

Weight management, as measured by body mass index and/or waist circumference, should be assessed on each visit. A body mass index of 18.5 to 24.9 kg per m<sup>2</sup> and a waist circumference (measured horizontally at the iliac crest) of less than 40 inches for men and less than 35 inches for women is recommended. (*Level of Evidence: B*) Additional weight management practices recommended include the following:

- a. On each patient visit, it is useful to consistently encourage weight maintenance/reduction through an appropriate balance of physical activity, caloric intake, and formal behavioral programs when indicated to maintain/achieve a body mass index between 18.5 and 24.9 kg per m<sup>2</sup>. (*Level of Evidence: B*)
- b. If waist circumference is 35 inches or more in women or 40 inches or more in men, it is beneficial to initiate lifestyle changes and consider treatment strategies for metabolic syndrome as indicated. (*Level of Evidence: B*)
- c. The initial goal of weight loss therapy should be to reduce body weight by approximately 10% from baseline. With success, further weight loss can be attempted if indicated through further assessment. (*Level of Evidence: B*)

### *Physical Activity*

#### *Class I*

1. The patient's risk after UA/NSTEMI should be assessed on the basis of an in-hospital determination of risk. A physical activity history or an exercise test to guide initial prescription is beneficial. (*Level of Evidence: B*)

2. Guided/modified by an individualized exercise prescription, patients recovering from UA/NSTEMI generally should be encouraged to achieve physical activity duration of 30 to 60 min per d, preferably 7 (but at least 5) d per week of moderate aerobic activity, such as brisk walking, supplemented by an increase in daily lifestyle activities (e.g., walking breaks at work, gardening, and household work). (*Level of Evidence: B*)
3. Cardiac rehabilitation/secondary prevention programs are recommended for patients with UA/NSTEMI, particularly those with multiple modifiable risk factors and/or those moderate- to high-risk patients in whom supervised exercise training is particularly warranted. (*Level of Evidence: B*)

### *Class IIb*

The expansion of physical activity to include resistance training on 2 d per week may be reasonable. (*Level of Evidence: C*)

### *Patient Education*

#### *Class I*

Beyond the detailed instructions for daily exercise, patients should be given specific instruction on activities (e.g., heavy lifting, climbing stairs, yard work, and household activities) that are permissible and those that should be avoided. Specific mention should be made regarding resumption of driving, return to work, and sexual activity. (*Level of Evidence: C*) Specific recommendations for physical activity are listed in section 5.4 in the original guideline document.

### *Influenza*

#### *Class I*

An annual influenza vaccination is recommended for patients with cardiovascular disease. (*Level of Evidence: B*)

### *Depression*

#### *Class IIa*

It is reasonable to consider screening UA/NSTEMI patients for depression and refer/treat when indicated. (*Level of Evidence: B*)

### *Nonsteroidal Anti-Inflammatory Drugs*

#### *Class I*

At the time of preparation for hospital discharge, the patient's need for treatment of chronic musculoskeletal discomfort should be assessed, and a stepped-care approach to treatment should be used for selection of treatments (See Figure 21 in the original guideline document). Pain relief should begin with acetaminophen, small doses of narcotics, or nonacetylated salicylates. (*Level of Evidence: C*)

### *Class IIa*

It is reasonable to use nonselective NSAIDs, such as naproxen, if initial therapy with acetaminophen, small doses of narcotics, or nonacetylated salicylates is insufficient. (*Level of Evidence: C*)

### *Class IIb*

Nonsteroidal anti-inflammatory drugs with increasing degrees of relative COX-2 selectivity may be considered for pain relief only for situations in which intolerable discomfort persists despite attempts at stepped-care therapy with acetaminophen, small doses of narcotics, nonacetylated salicylates, or nonselective NSAIDs. In all cases, the lowest effective doses should be used for the shortest possible time. (*Level of Evidence: C*)

### *Class III*

Nonsteroidal anti-inflammatory drugs with increasing degrees of relative COX-2 selectivity should not be administered to UA/NSTEMI patients with chronic musculoskeletal discomfort when therapy with acetaminophen, small doses of narcotics, nonacetylated salicylates, or nonselective NSAIDs provides acceptable levels of pain relief. (*Level of Evidence: C*)

### *Hormone Therapy*

#### *Class III*

1. Hormone therapy with estrogen plus progestin, or estrogen alone, should not be given de novo to postmenopausal women after UA/NSTEMI for secondary prevention of coronary events. (*Level of Evidence: A*)
2. Postmenopausal women who are already taking estrogen plus progestin, or estrogen alone, at the time of UA/NSTEMI in general should not continue hormone therapy. However, women who are more than 1 to 2 years past the initiation of hormone therapy who wish to continue such therapy for another compelling indication should weigh the risks and benefits, recognizing the greater risk of cardiovascular events and breast cancer (combination therapy) or stroke (estrogen). Hormone therapy should not be continued while patients are on bedrest in the hospital. (*Level of Evidence: B*)

### *Antioxidant Vitamins and Folic Acid*

#### *Class III*

1. Antioxidant vitamin supplements (e.g., vitamins E, C, or beta carotene) should not be used for secondary prevention in UA/NSTEMI patients. (*Level of Evidence: A*)
2. Folic acid, with or without B6 and B12, should not be used for secondary prevention in UA/NSTEMI patients. (*Level of Evidence: A*)

### **Postdischarge Follow-Up**

### *Class I*

1. Detailed discharge instructions for post-UA/NSTEMI patients should include education on medications, diet, exercise, and smoking cessation counseling (if appropriate), referral to a cardiac rehabilitation/secondary prevention program (when appropriate), and the scheduling of a timely follow-up appointment. Low-risk medically treated patients and revascularized patients should return in 2 to 6 weeks, and higher risk patients should return within 14 d. (*Level of Evidence: C*)
2. Patients with UA/NSTEMI managed initially with a conservative strategy who experience recurrent signs or symptoms of UA or severe (Canadian Cardiovascular Society class III) chronic stable angina despite medical management who are suitable for revascularization should undergo timely coronary angiography. (*Level of Evidence: B*)
3. Patients with UA/NSTEMI who have tolerable stable angina or no anginal symptoms at follow-up visits should be managed with long-term medical therapy for stable CAD. (*Level of Evidence: B*)
4. Care should be taken to establish effective communication between the post-UA/NSTEMI patient and health care team members to enhance long-term compliance with prescribed therapies and recommended lifestyle changes. (*Level of Evidence: B*)

## **Cardiac Rehabilitation**

### *Class I*

Cardiac rehabilitation/secondary prevention programs, when available, are recommended for patients with UA/NSTEMI, particularly those with multiple modifiable risk factors and those moderate- to high-risk patients in whom supervised or monitored exercise training is warranted. (*Level of Evidence: B*)

## **Special Groups**

### **Women**

### *Class I*

1. Women with UA/NSTEMI should be managed with the same pharmacological therapy as men both in the hospital and for secondary prevention, with attention to antiplatelet and anticoagulant doses based on weight and renal function; doses of renally cleared medications should be based on estimated creatinine clearance. (*Level of Evidence: B*)
2. Recommended indications for noninvasive testing in women with UA/NSTEMI are similar to those for men. (*Level of Evidence: B*)
3. For women with high-risk features, recommendations for invasive strategy are similar to those of men. (See Section 3.3 in the original guideline document and "Initial Conservative Versus Initial Invasive Strategies" section, above). (*Level of Evidence: B*)
4. In women with low-risk features, a conservative strategy is recommended. (*Level of Evidence: B*)

## **Diabetes Mellitus**

### *Class I*

1. Medical treatment in the acute phase of UA/NSTEMI and decisions on whether to perform stress testing, angiography, and revascularization should be similar in patients with and without diabetes mellitus. (*Level of Evidence: A*)
2. In all patients with diabetes mellitus and UA/NSTEMI, attention should be directed toward aggressive glycemic management in accordance with current standards of diabetes care endorsed by the American Diabetes Association and the American College of Endocrinology. Goals of therapy should include a preprandial glucose target of less than 110 mg per dL and a maximum daily target of less than 180 mg per dL. The postdischarge goal of therapy should be HbA1C less than 7%, which should be addressed by primary care and cardiac caregivers at every visit. (*Level of Evidence: B*)
3. An intravenous platelet GP IIb/IIIa inhibitor should be administered for patients with diabetes mellitus as recommended for all UA/NSTEMI patients (See Section 3.2 in the original guideline document and "Recommendations for Antiplatelet/Anticoagulant Therapies in Patients for Whom Diagnosis of UA/NSTEMI Is Likely or Definite" section, above). (*Level of Evidence: A*) The benefit may be enhanced in patients with diabetes mellitus. (*Level of Evidence: B*)

### *Class IIa*

1. For patients with UA/NSTEMI and multivessel disease, CABG with use of the internal mammary arteries can be beneficial over PCI in patients being treated for diabetes mellitus. (*Level of Evidence: B*)
2. Percutaneous coronary intervention is reasonable for UA/NSTEMI patients with diabetes mellitus with single-vessel disease and inducible ischemia. (*Level of Evidence: B*)
3. In patients with UA/NSTEMI and diabetes mellitus, it is reasonable to administer aggressive insulin therapy to achieve a glucose less than 150 mg per dL during the first 3 hospital (intensive care unit) days and between 80 and 110 mg per dL thereafter whenever possible. (*Level of Evidence: B*)

See Section 4 in the original guideline document for further explanation of revascularization strategies.

## **Post-CABG Patients**

### *Class I*

1. Medical treatment for UA/NSTEMI patients after CABG should follow the same guidelines as for non-post-CABG patients with UA/NSTEMI. (*Level of Evidence: C*)
2. Because of the many anatomic possibilities that might be responsible for recurrent ischemia, there should be a low threshold for angiography in post-CABG patients with UA/NSTEMI. (*Level of Evidence: C*)

### *Class IIa*

1. Repeat CABG is reasonable for UA/NSTEMI patients with multiple SVG stenoses, especially when there is significant stenosis of a graft that supplies the LAD. Percutaneous coronary intervention is reasonable for focal saphenous vein stenosis. (*Level of Evidence: C*) (Note that an intervention on a native vessel is generally preferable to that on a vein graft that supplies the same territory, if possible.)
2. Stress testing with imaging in UA/NSTEMI post-CABG patients is reasonable. (*Level of Evidence: C*)

## **Older Adults**

### *Class I*

1. Older patients with UA/NSTEMI should be evaluated for appropriate acute and long-term therapeutic interventions in a similar manner as younger patients with UA/NSTEMI. (*Level of Evidence: A*)
2. Decisions on management of older patients with UA/NSTEMI should not be based solely on chronologic age but should be patient-centered, with consideration given to general health, functional and cognitive status, comorbidities, life expectancy, and patient preferences and goals. (*Level of Evidence: B*)
3. Attention should be given to appropriate dosing (i.e., adjusted by weight and estimated creatinine clearance) of pharmacological agents in older patients with UA/NSTEMI, because they often have altered pharmacokinetics (due to reduced muscle mass, renal and/or hepatic dysfunction, and reduced volume of distribution) and pharmacodynamics (increased risks of hypotension and bleeding). (*Level of Evidence: B*)
4. Older UA/NSTEMI patients face increased early procedural risks with revascularization relative to younger patients, yet the overall benefits from invasive strategies are equal to or perhaps greater in older adults and are recommended. (*Level of Evidence: B*)
5. Consideration should be given to patient and family preferences, quality-of-life issues, end-of-life preferences, and sociocultural differences in older patients with UA/NSTEMI. (*Level of Evidence: C*)

## **Chronic Kidney Disease**

### *Class I*

1. Creatinine clearance should be estimated in UA/NSTEMI patients and the doses of renally cleared drugs should be adjusted appropriately. (*Level of Evidence: B*)
2. In chronic kidney disease patients undergoing angiography, isosmolar contrast agents are indicated and are preferred. (*Level of Evidence: A*)

## **Cocaine and Methamphetamine Users**

### *Class I*

1. Administration of sublingual or intravenous NTG and intravenous or oral calcium antagonists is recommended for patients with ST-segment elevation

- or depression that accompanies ischemic chest discomfort after cocaine use. (*Level of Evidence: C*)
2. Immediate coronary angiography, if possible, should be performed in patients with ischemic chest discomfort after cocaine use whose ST segments remain elevated after NTG and calcium antagonists; PCI is recommended if occlusive thrombus is detected. (*Level of Evidence: C*)
  3. Fibrinolytic therapy is useful in patients with ischemic chest discomfort after cocaine use if ST segments remain elevated despite NTG and calcium antagonists, if there are no contraindications, and if coronary angiography is not possible. (*Level of Evidence: C*)

#### *Class IIa*

1. Administration of NTG or oral calcium channel blockers can be beneficial for patients with normal ECGs or minimal ST-segment deviation suggestive of ischemia after cocaine use. (*Level of Evidence: C*)
2. Coronary angiography, if available, is probably recommended for patients with ischemic chest discomfort after cocaine use with ST-segment depression or isolated T-wave changes not known to be previously present and who are unresponsive to NTG and calcium antagonists. (*Level of Evidence: C*)
3. Management of UA/NSTEMI patients with methamphetamine use similar to that of patients with cocaine use is reasonable. (*Level of Evidence: C*)

#### *Class IIb*

Administration of combined alpha- and beta-blocking agents (e.g., labetalol) may be reasonable for patients after cocaine use with hypertension (systolic blood pressure greater than 150 mm Hg) or those with sinus tachycardia (pulse greater than 100 beats per min) provided that the patient has received a vasodilator, such as NTG or a calcium antagonist, within close temporal proximity (i.e., within the previous hour). (*Level of Evidence: C*)

#### *Class III*

Coronary angiography is not recommended in patients with chest pain after cocaine use without ST-segment or T-wave changes and with a negative stress test and cardiac biomarkers. (*Level of Evidence: C*)

### **Variant (Prinzmetal's) Angina**

#### *Class I*

1. Diagnostic investigation is indicated in patients with a clinical picture suggestive of coronary spasm, with investigation for the presence of transient myocardial ischemia and ST-segment elevation during chest pain. (*Level of Evidence: A*)
2. Coronary angiography is recommended in patients with episodic chest pain accompanied by transient ST-segment elevation. (*Level of Evidence: B*)
3. Treatment with nitrates and calcium channel blockers is recommended in patients with variant angina whose coronary angiogram shows no or nonobstructive coronary artery lesions. Risk factor modification is



recommended, with patients with atherosclerotic lesions considered to be at higher risk. (*Level of Evidence: B*)

#### *Class IIb*

1. Percutaneous coronary intervention may be considered in patients with chest pain and transient ST-segment elevation and a significant coronary artery stenosis. (*Level of Evidence: B*)
2. Provocative testing may be considered in patients with no significant angiographic CAD and no documentation of transient ST-segment elevation when clinically relevant symptoms possibly explained by coronary artery spasm are present. (*Level of Evidence: C*)

#### *Class III*

Provocative testing is not recommended in patients with variant angina and high-grade obstructive stenosis on coronary angiography. (*Level of Evidence: B*)

### **Cardiovascular "Syndrome X"**

#### *Class I*

1. Medical therapy with nitrates, beta blockers, and calcium channel blockers, alone or in combination, is recommended in patients with cardiovascular syndrome X. (*Level of Evidence: B*)
2. Risk factor reduction is recommended in patients with cardiovascular syndrome X. (*Level of Evidence: B*)

#### *Class IIb*

1. Intracoronary ultrasound to assess the extent of atherosclerosis and rule out missed obstructive lesions may be considered in patients with syndrome X. (*Level of Evidence: B*)
2. If no ECGs during chest pain are available and coronary spasm cannot be ruled out, coronary angiography and provocative testing with acetylcholine, adenosine, or methacholine and 24-h ambulatory ECG may be considered. (*Level of Evidence: C*)
3. If coronary angiography is performed and does not reveal a cause of chest discomfort, and if syndrome X is suspected, invasive physiological assessment (i.e., coronary flow reserve measurement) may be considered. (*Level of Evidence: C*)
4. Imipramine or aminophylline may be considered in patients with syndrome X for continued pain despite implementation of Class I measures. (*Level of Evidence: C*)
5. Transcutaneous electrical nerve stimulation and spinal cord stimulation for continued pain despite the implementation of Class I measures may be considered for patients with syndrome X. (*Level of Evidence: B*)

#### *Class III*

Medical therapy with nitrates, beta blockers, and calcium channel blockers for patients with noncardiac chest pain is not recommended. (*Level of Evidence: C*)

**Definitions:**

**Applying Classification of Recommendations and Level of Evidence**

		SIZE OF TREATMENT EFFECT		
		CLASS I	CLASS IIa	CLASS IIb
		<i>Benefit &gt;&gt;&gt; Risk</i>  Procedure/Treatment <b>SHOULD</b> be performed/administered	<i>Benefit &gt;&gt; Risk</i> <i>Additional studies with focused objectives needed</i>  <b>IT IS REASONABLE</b> to perform procedure/administer treatment	<i>Benefit ≥ Risk</i> <i>Additional studies with focused objectives needed</i> <i>registry or observational study may be helpful</i>  Procedure/Treatment <b>BE CONSIDERED</b>
<b>Estimate of Certainty (Precision) of Treatment Effect</b>	<b>LEVEL A</b>  Multiple (3–5) population risk strata evaluated*  General consistency of direction and magnitude of effect	<ul style="list-style-type: none"> <li>Recommendation that procedure or treatment is useful/effective</li> <li>Sufficient evidence from multiple randomized trials or meta-analyses</li> </ul>	<ul style="list-style-type: none"> <li>Recommendation in favor of treatment of procedure being useful/effective</li> <li>Some conflicting evidence from multiple randomized trials or meta-analyses</li> </ul>	<ul style="list-style-type: none"> <li>Recommendation in favor of treatment of procedure being useful/effective</li> <li>Some conflicting evidence from multiple randomized trials or meta-analyses</li> </ul>
	<b>LEVEL B</b>  Limited (2–3) population risk strata evaluated*	<ul style="list-style-type: none"> <li>Recommendation that procedure or treatment is useful/effective</li> <li>Limited evidence from single randomized trial or nonrandomized studies</li> </ul>	<ul style="list-style-type: none"> <li>Recommendation in favor of treatment of procedure being useful/effective</li> <li>Some conflicting evidence from single randomized trial or nonrandomized studies</li> </ul>	<ul style="list-style-type: none"> <li>Recommendation in favor of treatment of procedure being useful/effective</li> <li>Some conflicting evidence from single randomized trial or nonrandomized studies</li> </ul>

		SIZE OF TREATMENT EFFECT		
		CLASS I	CLASS IIa	CLASS IIb
		<i>Benefit &gt;&gt;&gt; Risk</i>  Procedure/Treatment <b>SHOULD</b> be performed/administered	<i>Benefit &gt;&gt; Risk</i> <i>Additional studies with focused objectives needed</i>  <b>IT IS REASONABLE</b> to perform procedure/administer treatment	<i>Benefit ≥ Risk</i> <i>Additional studies with focused objectives needed</i> <i>registry or randomized trial would be helpful</i>  Procedure/Treatment <b>COULD</b> be considered
LEVEL	LEVEL C	<ul style="list-style-type: none"> <li>Recommendation that procedure or treatment is useful/effective</li> <li>Only expert opinion, case studies, or standard-of-care</li> </ul>	<ul style="list-style-type: none"> <li>Recommendation in favor of treatment of procedure being useful/effective</li> <li>Only diverging expert opinion, case studies, or standard-of-care</li> </ul>	<ul style="list-style-type: none"> <li>Recommendation against treatment of procedure being useful/effective</li> <li>Only diverging expert opinion, case studies, or standard-of-care</li> </ul>

\*Data available from clinical trials or registries about the usefulness/efficacy in different subpopulations, such as gender, age, history of diabetes, history of prior myocardial infarction, history of heart failure, and prior aspirin use. A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Even though randomized trials are not available, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

NOTE: In 2003, the American College of Cardiology/American Heart Association (ACC/AHA) Task Force on Practice Guidelines developed a list of suggested phrases to use when writing recommendations. All guideline recommendations have been written in full sentences that express a complete thought, such that a recommendation, even if separated and presented apart from the rest of the document (including headings above sets of recommendations), would still convey the full intent of the recommendation. It is hoped that this will increase readers' comprehension of the guidelines and will allow queries at the individual recommendation level. (See Table 1 in the original guideline document for a list of suggested phrases for writing recommendations.)

## CLINICAL ALGORITHM(S)

Algorithms are provided in the original guideline document for:

- Evaluation and Management of Patients Suspected of Having Acute Coronary Syndrome (ACS)
- Patients With Unstable Angina/Non-ST-Elevation Myocardial Infarction (UA/NSTEMI) Managed by an Initial Invasive Strategy
- Patients With UA/NSTEMI Managed by an Initial Conservative Strategy
- Management After Diagnostic Angiography in Patients With UA/NSTEMI
- Long-Term Anticoagulant Therapy at Hospital Discharge After UA/NSTEMI
- Revascularization Strategy in UA/NSTEMI

## EVIDENCE SUPPORTING THE RECOMMENDATIONS

### REFERENCES SUPPORTING THE RECOMMENDATIONS

[References open in a new window](#)

### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

## BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

### POTENTIAL BENEFITS

Appropriate management of patients with unstable angina/non-ST-elevation myocardial infarction

### POTENTIAL HARMS

#### Calcium Antagonists

Major side effects include hypotension, worsening heart failure, bradycardia, and atrioventricular block.

#### Ticlopidine

The adverse effects of ticlopidine limit its usefulness: gastrointestinal problems (diarrhea, abdominal pain, nausea, and vomiting), neutropenia in approximately 2.4% of patients, severe neutropenia in 0.8% of patients, and, rarely, thrombotic thrombocytopenia purpura. Neutropenia usually resolves within 1 to 3 weeks of discontinuation of therapy but very rarely may be fatal. Thrombotic thrombocytopenia purpura, which is a very uncommon, life-threatening complication, requires immediate plasma exchange.

#### Clopidogrel

Clopidogrel carries the risk of both major and minor bleeding.

#### Anticoagulants, Including Heparin

Bleeding (major and minor) and heparin-induced thrombocytopenia are potential complications.

#### Glycoprotein IIb/IIIa Inhibitors

Treatment with glycoprotein IIb/IIIa antagonists increases the risk of bleeding, which is typically mucocutaneous or involves the access site of vascular intervention. Thrombocytopenia is an unusual complication of this class of agents.

## **Nitrates**

Side effects of nitroglycerine include headache and hypotension.

## **Morphine Sulfate**

Side effects of morphine sulfate include hypotension (especially in the presence of volume depletion and/or vasodilator therapy), nausea and vomiting, and respiratory depression.

## **Aspirin**

Gastrointestinal side effects such as dyspepsia and nausea are infrequent with the low doses. Primary prevention trials have reported a small excess in intracranial bleeding, which is offset in secondary prevention trials by the prevention of ischemic stroke.

## **Coronary Revascularization Procedures**

All revascularization procedures carry the risk of intraoperative and postoperative complications, including death.

# **CONTRAINDICATIONS**

## **CONTRAINDICATIONS**

- Patients with marked first-degree atrioventricular block, any form of second- or third-degree atrioventricular block in the absence of a functioning pacemaker, a history of asthma, severe left ventricular dysfunction or heart failure, or at high risk for shock should not receive beta-blockers on an acute basis. Patients with evidence of a low-output state (e.g., oliguria) or sinus tachycardia, which often reflects low stroke volume, significant sinus bradycardia (heart rate less than 50 beats per min), or hypotension (systolic blood pressure less than 90 mm Hg) should not receive acute beta-blocker therapy until these conditions have resolved. Patients with significant chronic obstructive pulmonary disease (COPD) who may have a component of reactive airway disease should be given beta-blockers very cautiously; initially, low doses of a beta-1-selective agent should be used.
- Rapid-release, short-acting dihydropyridines (e.g., nifedipine) must be avoided in the absence of concomitant beta-blockade because of increased adverse outcomes. Verapamil and diltiazem should be avoided in patients with pulmonary edema or evidence of severe left ventricular dysfunction.
- Contraindications to aspirin (ASA) include intolerance and allergy (primarily manifested as asthma with nasal polyps), active bleeding, hemophilia, active retinal bleeding, severe untreated hypertension, an active peptic ulcer, or another serious source of gastrointestinal or genitourinary bleeding.
- Acute fibrinolytic therapy is contraindicated for acute coronary syndrome (ACS) patients without ST-segment elevation, except for those with electrocardiographic true posterior myocardial infarction (MI) manifested as ST-segment depression in 2 contiguous anterior precordial leads and/or isolated ST-segment elevation in posterior chest leads.

- Nitroglycerin (NTG) is contraindicated after the use of sildenafil within the previous 24 h or tadalafil within 48 h or with hypotension.
- Contraindications to morphine sulfate include hypotension and intolerance.
- The use of bile acid sequestrants is relatively contraindicated when triglycerides are greater than 200 mg per dL

## QUALIFYING STATEMENTS

### QUALIFYING STATEMENTS

- These practice guidelines are intended to assist health care providers in clinical decision making by describing a range of generally acceptable approaches for the diagnosis, management, and prevention of specific diseases or conditions. Clinical decision making should consider the quality and availability of expertise in the area where care is provided. These guidelines attempt to define practices that meet the needs of most patients in most circumstances. These guideline recommendations reflect a consensus of expert opinion after a thorough review of the available, current scientific evidence and are intended to improve patient care.
- Patient adherence to prescribed and agreed upon medical regimens and lifestyles is an important aspect of treatment. Prescribed courses of treatment in accordance with these recommendations will only be effective if they are followed. Since lack of patient understanding and adherence may adversely affect treatment outcomes, physicians and other health care providers should make every effort to engage the patient in active participation with prescribed medical regimens and lifestyles.
- If these guidelines are used as the basis for regulatory/payer decisions, the ultimate goal is quality of care and serving the patient's best interests. The ultimate judgment regarding care of a particular patient must be made by the health care provider and patient in light of all the circumstances presented by that patient. There are circumstances in which deviations from these guidelines are appropriate.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

### IMPLEMENTATION TOOLS

Clinical Algorithm  
Quick Reference Guides/Physician Guides  
Resources

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Living with Illness

### IOM DOMAIN

Effectiveness  
Patient-centeredness  
Timeliness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

Anderson JL, Adams CD, Antman EM, Bridges CR, Califf RM, Casey DE Jr, Chavey WE 2nd, Fesmire FM, Hochman JS, Levin TN, Lincoff AM, Peterson ED, Theroux P, Wenger NK, Wright RS, Smith SC Jr, Jacobs AK, Adams CD, Anderson JL, Antman EM, Halperin JL, Hunt SA, Krumholz HM, Kushner FG, Lytle BW, Nishimura R, Ornato JP, Page RL, Riegel B, American College of Cardiology, American Heart Association Task Force on Practice Guidelines (Writing Committee, American College of Emergency Physicians, Society for Cardiovascular Angiography and Interventions, Society of Thoracic Surgeons, American Association of Cardiovascular and Pulmonary Rehabilitation, Society for Academic Emergency Medicine. ACC/AHA 2007 guidelines for the management of patients with unstable angina/non-ST-Elevation myocardial infarction: a report of the American College of Cardiology. J Am Coll Cardiol 2007 Aug 14;50(7):e1-e157. [957 references] [PubMed](#)

### ADAPTATION

Not applicable: The guideline was not adapted from another source.

### DATE RELEASED

2000 (revised 2007 Aug 14)

### GUIDELINE DEVELOPER(S)

American College of Cardiology Foundation - Medical Specialty Society  
American Heart Association - Professional Association  
Society for Cardiovascular Angiography and Interventions - Medical Specialty Society  
Society of Thoracic Surgeons - Medical Specialty Society

### SOURCE(S) OF FUNDING

The American College of Cardiology Foundation and the American Heart Association. No outside funding is accepted.

## **GUIDELINE COMMITTEE**

American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Writing Committee to Revise the 2002 Guidelines for the Management of Patients With Unstable Angina/Non–ST-Elevation Myocardial Infarction

## **COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE**

*Task Force Members:* Sidney C. Smith, Jr, MD, FACC, FAHA, *Chair*; Alice K. Jacobs, MD, FACC, FAHA, *Vice-Chair*; Cynthia D. Adams, RN, PHD, FAHA; Jeffrey L. Anderson, MD, FACC, FAHA; Elliott M. Antman, MD, FACC, FAHA¶; Jonathan L. Halperin, MD, FACC, FAHA; Sharon A. Hunt, MD, FACC, FAHA; Harlan M. Krumholz, MD, FACC, FAHA; Frederick G. Kushner, MD, FACC, FAHA; Bruce W. Lytle, MD, FACC, FAHA; Rick Nishimura, MD, FACC, FAHA; Joseph P. Ornato, MD, FACC, FAHA\*\*; Richard L. Page, MD, FACC, FAHA; Barbara Riegel, DNSC, RN, FAHA

¶Immediate Past Chair

\*\*Former Task Force member during this writing effort

*Writing Committee Members:* Jeffrey L. Anderson, MD, FACC, FAHA, *Chair*; Cynthia D. Adams, RN, PHD, FAHA; Elliott M. Antman, MD, FACC, FAHA; Charles R. Bridges, SCD, MD, FACC, FAHA\*; Robert M. Califf, MD, MACC; Donald E. Casey, Jr, MD, MPH, MBA, FACP\*\*; William E. Chavey II, MD, MS#; Francis M. Fesmire, MD, FACEP##; Judith S. Hochman, MD, FACC, FAHA; Thomas N. Levin, MD, FACC, FSCA@I; A. Michael Lincoff, MD, FACC; Eric D. Peterson, MD, MPH, FACC, FAHA; Pierre Theroux, MD, FACC, FAHA; Nanette Kass Wenger, MD, FACC, FAHA; R. Scott Wright, MD, FACC, FAHA

\*Society of Thoracic Surgeons Representative

\*\*American College of Physicians Representative

#American Academy of Family Physicians Representative

##American College of Emergency Physicians Representative

@Society for Cardiovascular Angiography and Interventions Representative

## **FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST**

The American College of Cardiology/American Heart Association (ACC/AHA) Task Force on Practice Guidelines makes every effort to avoid any actual, potential, or perceived conflict of interest that may arise as a result of an industry relationship or personal interest of a member of the Writing Committee. Specifically, all members of the Writing Committee, as well as peer reviewers of the document,



were asked to provide disclosure statements of all such relationships that may be perceived as real or potential conflicts of interest. Writing Committee members are also strongly encouraged to declare a previous relationship with industry that may be perceived as relevant to guideline development. If a Writing Committee member develops a new relationship with industry during their tenure, they are required to notify guideline staff in writing. The continued participation of the Writing Committee member will be reviewed. These statements are reviewed by the parent task force, reported orally to all members of the Writing Committee at each meeting, and updated and reviewed by the Writing Committee as changes occur. Please refer to the methodology manual for ACC/AHA Guideline Writing Committees further description of relationships with industry policy, available on the ACC and AHA World Wide Web sites (<http://www.acc.org/qualityandscience/clinical/manual/manual%5Fi.htm> and <http://www.circ.ahajournals.org/manual/>). See Appendix 1 in the original guideline document for a list of Writing Committee member relationships with industry and Appendix 2 in the original guideline document for a listing of peer reviewer relationships with industry that are pertinent to this guideline.

## **ENDORSER(S)**

American Association of Cardiovascular and Pulmonary Rehabilitation - Medical Specialty Society  
American College of Emergency Physicians - Medical Specialty Society  
Society for Academic Emergency Medicine - Medical Specialty Society

## **GUIDELINE STATUS**

This is the most current release of the guideline.

This guideline updates a previous version: American College of Cardiology Foundation, American Heart Association. ACC/AHA guidelines for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Bethesda (MD): American College of Cardiology Foundation (ACCF); 2002 Mar. 95 p.

## **GUIDELINE AVAILABILITY**

Electronic copies: Available from the [American College of Cardiology \(ACC\) Web site](#) and from the [American Heart Association \(AHA\) Web site](#).

Print copies: Available from the American College of Cardiology, Resource Center, 9111 Old Georgetown Rd, Bethesda, MD 20814-1699.

## **AVAILABILITY OF COMPANION DOCUMENTS**

The following is available:

- ACC/AHA 2007 guidelines for the management of patients with unstable angina/non-ST-elevation myocardial infarction—executive summary. 2007 Aug 14. 75 p.

Electronic copies: Available from the [American College of Cardiology Web site](#).

Print copies: Available from the American College of Cardiology, Resource Center, 9111 Old Georgetown Rd, Bethesda, MD 20814-1699.

Additionally, risk-calculator for 6-month postdischarge mortality after hospitalization for acute coronary syndrome is available in the [original guideline document](#).

## **PATIENT RESOURCES**

None available

## **NGC STATUS**

This summary was completed by ECRI on January 30, 2001. It was verified by the guideline developer as of April 27, 2001. This summary was updated on October 3, 2002. The updated information was verified by the guideline developer on June 9, 2003. This summary was updated by ECRI on March 6, 2007 following the U.S. Food and Drug Administration (FDA) advisory on Coumadin (warfarin sodium). This summary was updated by ECRI Institute on June 22, 2007 following the U.S. Food and Drug Administration (FDA) advisory on heparin sodium injection. This summary was updated by ECRI Institute on July 12, 2007 following the U.S. Food and Drug Administration (FDA) advisory on Troponin-1 Immunoassay. This NGC summary was updated by ECRI Institute on October 24, 2007. The updated information was verified by the guideline developer on January 7, 2008. This summary was updated by ECRI Institute on March 14, 2008 following the updated FDA advisory on heparin sodium injection.

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Date Modified: 10/6/2008

